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TREATMENT OF PSORIASIS WITH LIPOTROPIC SUBSTANCES DERIVED FROM FOODSTUFFS

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PSORIASIS AS A DISTURBANCE OF LIPID METABOLISM

The conception of psoriasis as a metabolic disturbance of the skin has received increasing support in recent years. Madden's excellent histologic study [1] of the uninvolved skin of patients with acute guttate and generalized papular psoriasis has strengthened greatly the concept of this disease as a disturbance of fat metabolism. The histologic changes which Madden found in the uninvolved skin but at the sites of election for psoriasis were: an increase of extracellular fat around the pilosebaceous apparatus and sweat glands and throughout the corium and a constant leukocytic infiltrate in the papillary bodies and in the upper half of the cutis. When the infiltrate was great the capillaries were dilated and engorged and the papillary bodies elongated and pushed toward the surface. These findings confirmed and extended those of Kartamyshev.[2] One is tempted to conclude that the difference between the apparently uninvolved and clinically psoriatic skin is only a matter of lowered threshold. It may be dependent either on local conditions in the skin or on the severity of the metabolic process. The tendency of psoriasis to occur on the elbows and knees may be due to factors peculiar to these areas, such as mechanical injury, stretching of the skin or lowered oxygen supply.

Madden's studies also explain the Koebner phenomenon that appears after mechanical, chemical and actinic trauma to the apparently normal skin of a patient with psoriasis, particularly in the eruptive stage. This phenomenon exhibited in psoriasis may be likened to the cutaneous

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1. Madden, J. F.: Histologic Studies of Uninvolved Skin of Patients with Psoriasis, Arch. Dermat. & Syph. **44**:655 (Oct.) 1941.

2. Kartamyshev, A. I.: Histologic Character of Apparently Healthy Skin in Psoriatic Patients, abstracted, Arch. Dermat. & Syph. **40**:813 (Nov.) 1939.

changes in pellagra and is particularly pertinent since pellagra represents a metabolic disturbance brought about by a vitamin deficiency. Here again the cutaneous lesions are precipitated by exposure to sunlight on exposed areas and by friction or stretching of the skin on unexposed parts of the body. After extensive histologic and clinical investigations Grütz and Burger [3] came to the conclusion that psoriasis was a lipoidosis. This belief was based on the increased lipids in the serum and cutaneous lesions of the patient with psoriasis and the favorable response to the prolonged use of a diet low in fat. There have been considerable disagreement in the reports [4] on the amount of cholesterol in the serum of patients with psoriasis but slight difference of opinion on the value of the Grütz diet. It should be remembered, however, that the term fat metabolism as applied to neutral fats, unsaturated fatty acids, phospholipids and sterols may include interdependent but quite possibly independent processes. An alteration of these processes does not necessarily have to express itself by an increase in serum cholesterol or total lipids, for as extensive a lipid disturbance as xanthomatosis may be associated with a normal cholesterol content of the serum. The reported lack of response to the Grütz low fat diet may well be due to the difficulties encountered in maintaining the diet for ambulatory patients. A reduced intake of lipids, which may lessen the strain on an impaired metabolic mechanism, does not restore conditions to normal or correct the essential defect in enzymatic and hormonal functions. It is analogous to the low carbohydrate regimen for diabetes, which can cope only with a certain degree of insulin deficiency.

A considerable achievement in the experimental study of fat metabolism has been the recognition of choline as an important lipotropic substance.[5] Another successful step forward in this research was the establishment of lipocaic as a lipotropic hormone of the pancreas.[6] The promising results obtained by Clark, Dragstedt and Becker [7] in the treatment of psoriasis again confirm the view that psoriasis is concerned with fat metabolism. Since modern biochemistry has firmly established

3. Grütz, O., and Burger, M.: Die Psoriasis als Stoffwechselproblem, Klin. Wchnschr. **12**:373 (March 11) 1933. Grütz, O.: Neue histologische Beiträge zum Psoriasisproblem, Arch. f. Dermat. u. Syph. **177**:246 (May) 1938.

4. Statzierer, H.: Contributions à l'étude de la cholestérinémie et de la glycémie dans le psoriasis, Thesis, Paris, 1926, vol. 70. Colarusso, A.: La psoriasi come malattia del metabolismo dei lipoidi, Riforma med. **56**:271 (March) 1940.

5. Best, C. H., and Huntsman, M. E.: Effects of Components of Lecithine upon Deposition of Fat in Liver, J. Physiol. **75**:405 (Aug.) 1932. Best, C. H., and Ridout, J. H.: Annual Review of Biochemistry, Stanford University, Calif., Stanford University Press, 1941.

6. Dragstedt, L. R.: Present Status of Lipocaic, J. A. M. A. **114**:29 (Jan. 6) 1940.

7. Clark, D. E.; Dragstedt, L. R., and Becker, S. W.: Further Observations on the Use of Lipocaic in the Treatment of Psoriasis, J. Invest. Dermat. **4**:59 (Feb.) 1941.

that vitamins which supply the building stones for cellular enzymes are essential to the metabolism of fats, it seemed worth while to evaluate the therapeutic action of various vitamins on psoriasis from this point of view. This became particularly desirable after the fundamental work of McHenry and Gavin [8] on the production and prevention of cholesterol fatty livers in rats demonstrated a similarity in the action of lipocaic and substances identified as part of the vitamin B complex. These scientists found that a special fraction of aqueous liver extract would produce in rats fed a fat-free diet fatty livers which were not prevented or cured by choline. Experimentally produced fatty livers high in cholesterol were prevented or cured by giving lipocaic.

McHenry and Gavin also stated that yeast and rice polishings had the same effect on the cholesterol fatty livers of rats as lipocaic. Gross [9] described these findings as significant in the conception and treatment of psoriasis and reported good therapeutic results from parenteral liver therapy in 2 cases of psoriatic erythroderma.

Dramatic development in the experiments of McHenry and Gavin on fatty livers in rats established that the liver extract which produced cholesterol fatty livers owed its action to biotin. Of even greater significance was these authors' search for the substance in yeast, rice polishings, wheat germ and other natural products which, like lipocaic, prevented or cured biotin fatty livers in rats. It was indeed good fortune that at this time Woolley [10] described a vitamin deficiency in the mouse which presented as its predominant feature an extensive alopecia. Woolley isolated inositol as this anti-mouse-alopecia factor. Then Gavin and McHenry [11] proved that inositol was the substance in such natural sources of the vitamin B complex as liver, rice polishings and wheat germ that cured biotin fatty livers of rats. Woolley [12] also found inositol to be present in cereals, soybean phospholipids, wheat germ, liver extract, heart muscle and a number of other substances. Klenk and Sakai [13] had previously proved that soybean cephalin contained inositol in its structure. The recent discovery of Folch and

8. McHenry, E. W., and Gavin, G.: Effects of Beef Liver Fraction upon Fat Synthesis in Rats, Science **91**:171 (Feb. 16) 1940.

9. Gross, P., in discussion on Clark, Dragstedt and Becker.[7]

10. Woolley, D. W.: Nature of Anti-Alopecia Factor, Science **92**:384 (Oct. 25) 1940.

11. Gavin, G., and McHenry, E. W.: Inositol: A Lipotropic Factor, J. Biol. Chem. **139**:485 (May) 1941.

12. Woolley, D. W.: Study of Biological Specificity of Inositol, J. Biol. Chem. **140**:461 (Aug.) 1941.

13. Klenk, E., and Sakai, R.: Inositmonophosphorsaüre, ein Spaltprodukt der Sojabohnenphosphatide, Ztschr. f. physiol. Chem. **258**:33, 1939.

Woolley [14] of the structural integration of inositol in human cephalin may be of great significance in the study of phospholipid metabolism in man.

In later experiments Gavin and McHenry [15] concluded that cholin prevented the abnormal deposit of neutral fats in the liver of the rat which was caused by thiamine under certain experimental conditions, while lipocaic and inositol prevented the cholesterol fatty liver of the rat produced by the feeding of biotin. In addition to biotin, Engel [16] has shown that pantothenic acid and Forbes [17] that nicotinic acid is involved in the production of the cholesterol fatty liver in the rat. The delaying effect of linoleic and of arachidonic acid on the pyridoxine deficiency of the rat may well be concerned with fat metabolism, as suggested by Gross.[18]

POSSIBLE RELATION OF THE THERAPEUTIC EFFECT OF SOYBEAN LECITHIN AND DEFATTED WHEAT GERM TO CHOLINE AND INOSITOL

While we were engaged in the study of the therapeutic effect on psoriasis of crude natural vitamin B complex in the form of liver extract, yeast, rice polishings extract and wheat germ, our attention was called to another natural product derived from soybeans rich in cephalin and lecithin. This "soy bean lecithin" [19] was effective in reducing experimental cholesteremia in rabbits.[20] It was of course of particular interest when Woolley demonstrated that inositol, the anti-mouse-alopecia factor, was present in this soybean phospholipid. Thus a link was established between the substances that seemed effective in our hands in a small group of cases of psoriasis, namely, yeast, rice polishings, crude liver extract, defatted wheat germ and the soybean lecithin mixture. This mixture resembles lipocaic in its action, not only in its therapeutic effect

14. Folch, J., and Woolley, D. W.: Inositol: A Constituent of a Brain Phosphatide, J. Biol. Chem. **142**:963 (Feb.) 1942.

15. Gavin, G., and McHenry, E. W.: Effect of Biotin upon Fat Synthesis and Metabolism, J. Biol. Chem. **141**:619 (Nov.) 1941.

16. Engel, R. W.: Effect of Calcium Panthothenate and Other Vitamin B Factors on Liver Fat, J. Biol. Chem. **140**:37 (July) 1941.

17. Forbes, J. C.: Vitamin B Complex and Fat Metabolism, J. Nutrition **22**:359 (Oct.) 1941.

18. Gross, P.: Role of Unsaturated Fatty Acids in Acrodynia (Vitamin B_6 Deficiency) of Albino Rat, J. Invest. Dermat. **3**:505 (Dec.) 1940.

19. Soybean lecithin is made by the American Lecithin Company, Elmhurst, Long Island, N. Y. Analysis of granulated soybean lecithin shows approximately: lecithin, 20 per cent; cephalin, 20 per cent; crude inositol, 5 to 10 per cent; choline, 3 per cent; fats, 3 per cent, and traces of minerals, proteins and vitamins.

20. Meeker, D. R., and Kesten, H. D.: Experimental Atherosclerosis and High Protein Diets, abstracted, Proc. Soc. Exper. Biol. & Med. **45**:543 (Nov.) 1940.

in psoriasis but in its pronounced ability to reduce abnormally high serum cholesterol in patients with lipid disturbances. As shown in table 1, 5 patients with hypercholesteremia showed an appreciable reduction in the serum cholesterol after the ingestion of either soybean lecithin or wheat germ over varying periods.

In the course of these preliminary trials it became apparent that a special defatted wheat germ, "VioBin," [21] was superior in its antipsoriatic effect to yeast, liver and rice polishings concentrate and that it compared favorably with the action of soybean lecithin. Since the inositol content of this wheat germ is considerably lower than that of soybean lecithin, it seems probable that other factors, acting as catalysts, enhance the effect of inositol. The high content of manganese in this wheat

TABLE 1.—*Effect of Lipotropic Substances on Hypercholesteremia*

Patient	Diagnosis	Before Treatment: Serum Cholesterol, per 100 Cc.	Before Treatment: Blood Sugar, per 100 Cc.	Therapy	After Treatment, Serum Cholesterol, per 100 Cc.
A. T., aged 50	Xanthelasma	800 mg.	95 mg.	60 Gm. soybean lecithin daily for 5 weeks	225 mg.
				4 Gm. soybean lecithin daily for 16 weeks	467 mg.
R. A., aged 59	Extracellular cholesterosis	388 mg.	100 mg.	60 Gm. soybean lecithin daily for 3 months	190 mg.
C. C., aged 16	Necrobiosis lipoidica diabeticorum	400 mg.	300 mg.	45 Gm. soybean lecithin daily for 5 weeks; also diabetic regimen including insulin	215 mg.
A. M., aged 32	Psoriasis	325 mg.	Not tested	30 to 45 Gm. of VioBin daily for 4 months	227 mg.
E. S., aged 59	Nummular eczema	330 mg.	90 mg.	30 Gm. of VioBin daily for 6 weeks; also vitamin A and calcium	240 mg.

germ reminds one of the successful use of parenteral injections of colloidal manganese [22] in the treatment of psoriasis. The presence of a well balanced vitamin B complex in wheat germ and the presence of choline in soybean lecithin as well as in the vitamin B complex raise the question of the various factors which may be involved in the curative action of soybean lecithin and wheat germ. Furthermore, it is signifi-

21. VioBin is made by the VioBin Corporation, Monticello, Ill. An analysis of this product, a defatted, dehydrated wheat germ precooked at 85 F. for three hours, shows approximately: inositol, 2,500 micrograms per gram; thiamine, 33 micrograms per gram; riboflavin, 9 micrograms per gram; nicotinic acid, 79 micrograms per gram; pyridoxine, 15 micrograms per gram; pantothenic acid, 26 micrograms per gram; biotin, 0.450 microgram per gram; potassium, 1 per cent; phosphorus, 1 per cent; manganese, 0.3 per cent, and choline, an amount too small for biologic assay.

22. VanKerckhoff, J. H. P.: Beitrage zur Kenntnis der Psoriasis Vulgaris, Leipzig, S. Hirzel, 1929.

cant that although inositol exerts some lipotropic activity in depancreatized dogs it does not preserve life and its lipotropic effect is not as great as that secured by an identical amount of a preparation of lipocaic.[23]

RELATION OF VITAMINS TO METABOLISM AND THE USE OF VITAMINS B, C AND D IN PSORIASIS

Since the influence of vitamins on cell metabolism is well established, it seems of interest to review the literature on the treatment of psoriasis with other vitamins. Spiethoff [24] and Grüneberg [25] reported good results from the use of crude liver extract in the treatment of psoriasis. Madden [26] and Pulay [27] found the vitamin B complex or its components of benefit in psoriasis, particularly in combination with an endocrine preparation (extracts of pancreas, adrenal cortex or anterior lobe of pituitary), dilute hydrochloric acid or a low fat diet.

A summary of the literature on the treatment of psoriasis with ascorbic acid shows that of 89 patients treated with this vitamin over varying periods up to six months and in amounts up to 110 Gm. only 10 patients became free of lesions. The period of observation was either not given or unduly short.

A summary of the literature on vitamin D therapy in psoriasis reveals that 269 patients were treated with vitamin D preparations. All investigators, except Monash, gave massive doses of either the crystalline vitamin D or the natural fish oils. Of these 269 patients 45 became free of lesions. Again the period of observation was either not stated or was unduly short.

Judging from these reports, some therapeutic action on psoriasis must be conceded to the use of these vitamins. There are indications that the effects of these vitamins on psoriasis may be related to phospholipid metabolism rather than to the well established effects of vitamins C and D. It has been shown [28] that vitamin C can act as a catalyst for the oxidation of phospholipids. The role of vitamin D in psoriasis may

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23. Owens, F. M., Jr.; Allen, J. G.; Stingler, D., and Dragstedt, L. R.: The Comparative Effects of Inositol and Lipocaic in Depancreatized Dogs, read at the annual meeting of the American Physiological Society, Boston, 1942.

24. Spiethoff, B.: Erfahrungen mit der Lebertheraphie bei Intoxikationszuständen nach Salvarsan, Wismut, bei Infektionen und Psoriasis, München. med. Wchnschr. **76**:577 (April) 1929.

25. Grüneberg, T.: Die Lebertheraphie der Psoriasis, Dermat. Wchnschr. **97**:1793 (Dec. 9) 1933.

26. Madden, J. F.: Treatment of Psoriasis, J. A. M. A. **115**:588 (Aug. 24) 1940.

27. Pulay, E.: Le "psoriasis vulgaris," et son traitement, Bull. Soc. franç. de dermat. et syph. **43**:1508 (July) 1936.

28. Deutsch, H. F.; Kline, B. E., and Rusch, H. P.: Oxidation of Phospholipids in the Presence of Ascorbic Acid and Carcinogenic Chemicals, J. Biol. Chem. **141**:529 (Nov.) 1941.

be better understood from our viewpoint if its effect on phosphorus absorption is considered in addition to its better known action on calcium.[29] This and its fat solubility certainly link vitamin D with fat metabolism. Thacker [30] observed that a cod liver oil concentrate contained an unidentified antipsoriatic factor of greater potency than was present in other pure vitamin D preparations. It is of interest to speculate on whether this factor acts as a synergist or whether the massive doses of vitamin D used in psoriasis and arthritis owe their effect to a lipotropic substance. These speculations may be of value in supplying clues for continued research into the more complicated metabolic disturbances underlying the disease called psoriasis. It should also project into the psoriatic problem the well known fact that vitamins and hormones are closely interwoven in their action on metabolic processes and thus remove apparent contradictions in the approach to many medical problems of which psoriasis certainly is one.

The interrelation of vitamins and hormones can best be realized by studying the carbohydrate metabolism in diabetes mellitus. The part of thiamine as a building stone for cocarboxylase, that of nicotinic acid for coenzyme I and II and that of riboflavin for yellow enzyme and several other alloxazine proteins are well established. Yet, as Stadie [31] has pointed out, no specific process in carbohydrate catabolism can be definitely attributed to insulin, which as a hormone may have a catalytic effect on several phases of carbohydrate and fat metabolism.

DYSVITAMINOSIS AND CONSTITUTIONAL DISTURBANCES IN PSORIASIS, INCLUDING THE PROBLEM OF HEREDITY

The fact that certain substances in foods, which have been established as vitamins, have a beneficial effect on psoriasis should not produce the false impression that a dietary deficiency is responsible for the disease. This would be contradictory to all empiric knowledge about psoriasis, including that relating to heredity. Constitutional factors have to be postulated as a fundamental cause of psoriasis and these may concern particularly the system of endocrine glands and also the liver and the pancreas. That a congenital anomaly may produce a vitamin deficiency has been shown to be true in Darier's disease.[32] Although low vitamin A

29. Sherman, H. C.: Chemistry of Food and Nutrition, ed. 6, New York, The Macmillan Company, 1941, p. 433.

30. Thacker, E. A.: Vitamin D Preparations and Psoriasis, Illinois M. J. **78**:352 (Oct.) 1940.

31. Stadie, W. C.: Intermediary Metabolism in Diabetes Mellitus, in Harvey Lectures, Lancaster, Pa., The Science Press Printing Company, 1942, series 37, p. 165.

32. Peck, S. M.; Chargin, L., and Sobotka, H.: Keratosis Follicularis (Darier's Disease): Vitamin A Deficiency Disease, Arch. Dermat. & Syph. **43**:223 (Feb.) 1941.

levels in the blood, abnormal biophotometric readings and response to vitamin A therapy establish Darier's disease as a vitamin deficiency, the clinical and histologic pictures differ fundamentally from phrynoderma, the nutritional vitamin A deficiency. The example of Darier's disease demonstrates that a disease *sui generis* may develop as a result of the interaction of various contributing constitutional factors. Similar conditions probably account for the clinical picture of dermatoses developing in patients with the constitutional background of a status seborrhoeicus. Even those patients responding to parenteral therapy with the vitamin B complex differ clinically from those with nutritional deficiency states involving the vitamin B complex.

For further investigation of the problem of psoriasis we offer the following working hypothesis: The psoriatic diathesis is a constitutional disturbance which in a considerable percentage of cases is hereditary. The hereditary incidence of the constitutional anomaly predisposing to psoriasis is probably higher than that of psoriasis itself. The occurrence of a first attack of psoriasis well beyond middle age makes it probable that a latent psoriatic constitution may exist during lifetime without the development of psoriasis. More statistical data are desirable to show the incidence of diabetes mellitus in the ascendancy of psoriasis, but we believe there is an overlapping of these two diseases. The factors eliciting the first attack of psoriasis might be subdivided into the following groups: (1) factors aggravating the constitutional weakness, such as puberty, menopause, acute infections, chronic infections and climatic changes; (2) factors which lead to the clinical manifestations of the constitutional disturbance, such as an increase of the fat content of the diet, and (3) relative deficiency in nutritive factors required for satisfactory enzymatic functions.

REPORT OF CASES

The rapid developments which have taken place in the biochemistry of fat metabolism in the last few years are reflected in our clinical studies. We were first impressed by the value of the vitamin B complex in the treatment of a patient with generalized erythroderma psoriaticum presenting unusual features.

CASE 1.—Mrs. S. K., aged 65, was admitted to the Presbyterian Hospital on Jan. 7, 1940 because of a generalized eruption of one and one-half years' duration. Previous to that, for several years, she had been afflicted with an eruption which was confined to the armpits and submammary folds. She had received treatments by various physicians, consisting of topical applications, roentgen therapy, ultraviolet irradiation, vitamin therapy, autohemotherapy, spleen extract and diets, which resulted only in temporary improvement of a moderate degree.

On her admission the face, trunk and extremities were covered with a diffuse erythematous eruption and extensive scales. The exfoliation consisted of large lamellar scales, which, in conjunction with the dark red erythema, gave the

appearance of pityriasis rubra. Only the lower part of the back, the buttocks and the posterior surface of the right thigh were free of the eruption. The erythroderma showed no sharp demarcation against these areas of normal skin. The palms were normal, but the eruption had extended to the soles, which were covered with heavy micaceous scales. The dorsa of the hands and feet were diffusely red and scaly, and the lower third of the legs and the feet were edematous. The scalp was covered with whitish scales distributed in large patches, and the hair, regrown after a diffuse defluvium, was short. Several toe nails were discolored, and there were psoriasiform patches between the toes. The finger nails were normal.

The blood was normal; there were 102 per cent hemoglobin, 5,500,000 red cells and 11,800 white cells, of which 64 per cent were polymorphonuclear leukocytes, 24 per cent lymphocytes, 6 per cent monocytes, 4 per cent eosinophils and 2 per cent basophils. The blood sugar was 112 mg., the serum cholesterol 107 mg. and the serum protein 7.8 Gm. (albumin 4.8 Gm. and globulin 3.0 Gm.) per hundred cubic centimeters. There were 0.03 mg. of arsenic per hundred grams of dry blood and 0.014 mg. of arsenic in the twenty-four hour output of urine. The urine was free of sugar and albumin.

A section of the affected skin showed the histologic picture of a psoriasiform dermatitis with parakeratosis, localized superficial abscesses in the epidermis and extreme acanthosis. The rete pegs were elongated, and the corium was the site of an intense inflammatory reaction with polymorphonuclear leukocytes infiltrating the corium and epidermis. Edema of the epidermis and corium was pronounced.

In view of the exfoliative erythroderma, which was considered of psoriatic origin, the treatment consisted of: injections of crude liver extract in doses of 5 cc.; parenteral injections of thiamine hydrochloride in doses of 10 mg.; oral administration of riboflavin, 6 to 10 mg. daily, and wheat germ oil, 1 to 2 teaspoonfuls daily. This treatment was instituted on Jan. 10, 1941, and on February 2 the eruption had improved sufficiently so that the patient could leave the hospital. The erythema of the face was paler, the scaling of the scalp had diminished and the skin of the trunk and upper extremities was nearly normal, except the areas under the breasts and on the upper part of the abdomen. On the legs and feet and soles were large erythematous and scaly patches, typical of a localized psoriasis. There was great improvement of the general condition, and the patient, who had for a long time been bedridden and mentally depressed, presented a remarkable change. The treatment was continued with injections of liver extract and oral administration of riboflavin, nicotinic acid and wheat germ oil.

Local treatment consisted of application of an ointment containing aluminum acetate solution in an absorption base or boric acid ointment U. S. P. The lesions on the legs and feet were not responding to this treatment, and roentgen therapy was given, 475 r divided into seven doses from February 24 to April 11.

On March 28 oral administration of an aqueous liver extract was substituted for the parenteral therapy. Because of a mild coronary thrombosis, the patient was confined to her bed from May 4 on. On August 6 a rice polishings extract and yeast concentrate were prescribed. Tar and dihydroxyanthranol (anthralin) ointments were tried on the residual eruption, but their use could not be continued because of a hypersensitivity of the skin. During the autumn of 1940 the patient's eruption cleared up and the hair of the scalp regrew. She continued taking a rice polishings concentrate, and there was no recurrence of psoriatic lesions. When she was seen on May 29, 1942, her skin was normal except for a dermatophytosis of the toes. The nails showed no psoriatic changes, and the scalp was covered over with dark brown hair of normal fulness. Her physical condition and mental state were excellent, and she was able to do her own housework.

Since the oral administration of a crude aqueous liver extract proved effective in this patient, the findings of McHenry and Gavin dealing with the lipotropic action of crude vitamin B complex on cholesterol fatty livers in rats took on clinical significance. Their comparison of the action of yeast concentrate, rice polishings and like substances with that of lipocaic furnished a way for overcoming the difficulty of obtaining lipocaic even for experimental use. It was also noted that in case 2, a report of which follows, the psoriasis disappeared while massive doses of crude liver extract, yeast, ferrous sulfate and iron adenylate were being administered.

CASE 2.—E. McA., a man aged 52, was admitted to the Presbyterian Hospital on Jan. 13, 1941 on account of an eruption of seven months' duration. He had been working in an illuminating gas factory for the past twenty-three years. In the last six years he had been drinking, on an average, a pint (475 cc.) of rye whisky a day and had been eating at restaurants and irregularly. For the past year he had lost his appetite and suffered from occasional nausea and a great deal of flatulence. For the past six years he had had frequent attacks of vertigo, and for about two years he had noticed numbness of the legs from the knees down.

The family history was irrelevant except for the fact that three cousins had died from diabetes.

The eruption consisted of two types of lesions. The eruption on the face and ears was typical of lupus erythematosus and was associated with extensive lesions on the vermilion portions of the lips. The histologic examination of tissue taken from a lesion on the face showed characteristic changes of lupus erythematosus. On the scalp was an eruption of erythematous and scaly patches suggestive of psoriasis, and on the shins were large plaques of inveterate and scaly psoriasis. Smaller lesions were present on the thighs and on the trunk, especially on the back. A biopsy of tissue from a lesion on the legs proved the diagnosis of psoriasis.

Physical examination revealed a left-sided hypertrophy and enlargement of the heart. The left pupil was larger than the right. Knee jerks were absent, and there was a fibrillary twitching of the muscles of the legs. The liver was moderately enlarged. Analysis of the gastric contents suggested hypoacidity, with free hydrochloric acid amounting to 24 and the total acid to 30. The roentgenologic examination of the gastrointestinal tract showed no abnormalities.

Examination of the blood showed 14.8 Gm. of hemoglobin, 3,900,000 red cells, 278,000 platelets and 8,400 white cells, with 0.9 per cent reticulocytes, 55 per cent neutrophils, 21 per cent lymphocytes, 12 per cent eosinophils and 12 per cent monocytes. There was a slight anisocytosis. Repeated examinations of the blood showed a similar picture of a mild hyperchromic macrocytic anemia. Urinalysis showed a 2 plus reaction for albumin, with hyaline and finely granular casts. There was 0.133 mg. (133 micrograms) of coproporphyrin in a twenty-four hour specimen of urine, representing an almost 100 per cent increase in coproporphyrin. A test of hepatic function with bromsulphalein revealed a retention of 40 per cent after thirty minutes. A cephalin flocculation test performed by Dr. Hanger gave a 2 to 3 plus reaction, suggesting active irritation of the parenchyma of the liver. A chemical examination of the serum showed 3.4 Bodansky units of phosphatase and 4.2 mg of inorganic phosphorus, 11.4 mg. of calcium, 29 mg. of nonprotein nitrogen, 8.4 Gm. of protein (4.3 Gm. of albumin, 4.1 Gm. of globulin and 0.8 Gm. of euglobulin) and 260 mg. of cholesterol per hundred cubic centimeters.

The patient received twenty injections of 5 cc. of liver extract, brewers' yeast, 0.6 Gm. of ferrous sulfate per day and five injections of iron adenylate. This treatment resulted in decided improvement of the eruption of the lupus erythematosus as well as of the psoriasis. This coincided with an improvement of the liver function and a reduction of the serum cholesterol from 260 to 178 mg. per hundred cubic centimeters. There was no change in the albuminuria and only a slight change in the urinary coproporphyrin (133 micrograms per twenty-four hours to 120 micrograms).

By February 19 the eruption on the face had completely cleared up and the psoriatic lesions had disappeared except for residual pigmentation. On April 16 the patient's skin was found to be clear of eruptions but the lower lip was covered with patches of lupus erythematosus. His general health had improved, but he still complained of a tired feeling and numbness in his legs. There was a definite uncertainty in his gait, with a loss of vibratory sense in both feet. With large doses of thiamine hydrochloride and a synthetic vitamin B complex preparation of high potency there was further improvement, but the ataxia responded only after intravenous injections of pyridoxine. The lupus erythematosus also dis-

TABLE 2.—*The Results of Tests for Cholesterol Content and Cephalin Flocculation (Case 2)*

Date	Cholesterol, Mg. per 100 Cc.	Cephalin Flocculation
1/15/41	260	++ - +++
1/27/41	178	+ - ++
1/31/41	213	....
2/13/41	206	....
4/22/41	163	....
6/27/41	160	....
10/23/41	232	Negative

appeared after a series of injections of pyridoxine (100 mg.). A maintenance dose of yeast was then prescribed. The patient abstained from alcohol, and on November 12 he was found free from psoriasis and lupus erythematosus.

The addition of wheat germ to the therapy was surprisingly effective, as shown in cases 3, 4, 5 and 6.

CASE 3.—N. M., a man aged 28, a teacher, was first seen on April 1, 1941, complaining of an eruption on the hands and feet which had been present for the past five months.

The eruption consisted of sharply circumscribed erythematous and moderately scaly patches on both palms, the volar surfaces of all the fingers and the flexor surfaces of the wrists. On the periphery of many of these patches were deep-seated minute vesicles surrounded by slight erythema. The nails of the thumb, index, third and fifth fingers of the right hand and of the thumb, index and third fingers of the left hand were thickened, cloudy and scaly on the surface and showed transverse furrows. Otherwise, the normal nails showed scaling at their bases, and under the nail of the left middle finger were many subungual papules the size of a pinhead. On the tips of several toes of both feet and on the heels were circumscribed erythematous and scaly patches which were studded with small deep-seated vesicles. At the points of maximum pressure the scales were thick. The toe nails had lost their translucency but showed no thickening.

Scrapings and cultures for fungi from the nails were negative. The tonsils had been removed many years before, but there were small residues of adenoid tissue in both tonsillar fossae. Examination of the blood showed nothing abnormal.

The condition was slightly improved by application of 10 per cent of colloidal juniper tar, but new deep-seated pustules were developing in and around the lesions on the palms.

On April 11 the patient was given yeast concentrate, a rice polishing preparation, 25 mg. of pyridoxine per day and 1 teaspoon of wheat germ oil twice a day. Local treatment was continued. On April 21 the eruption had greatly improved and only a few vesicles were present in the lesions of the palms. By May 16 the eruption had completely cleared and the patient was advised to take defatted wheat germ and a yeast concentrate. On June 9 he was seen on account of a mild dermatophytosis between the toes. The patient continued to take 2 teaspoonfuls of defatted wheat germ, and when he was seen on November 27 there had been no recurrence of pustular psoriasis. The finger nails had improved but still showed some pitting and furrows. On March 13, 1942 he was again examined and the only evidence of psoriasis was a dime-sized patch, slightly red and scaly, on the tip of the third finger of the right hand. The finger nails were of normal thickness, but there were still some transverse furrows and pitting. Between the toes were macerated and scaly patches, and on the soles were a few dried vesicles. A microscopic examination of material from the lesions on the soles showed typical mycelium. The examination of the blood on March 18 showed 248 mg. of cholesterol per hundred cubic centimeters of blood. Therapy with defatted wheat germ was continued. By April 24 the psoriatic patch on the tip of the right middle finger had healed. There was still a slightly hyperkeratotic patch on the tip of the index finger, but otherwise no psoriasis was present.

Case 4.—H. G. B., a man aged 37, was seen on June 14, 1941, with an eruption of twenty-four years' duration. During this period he had never been entirely free of this eruption, but the condition usually improved during the fall or winter. He had not responded to roentgen ray therapy or exposure to the sun and had found various topical applications, including coal tar ointments, of no value. He had improved two years before under treatment with vitamins and liver extract. His father had had psoriasis, and two sisters had been subject to diseases of the skin.

The eruption consisted of large erythematous scaly and somewhat infiltrated patches measuring up to 4 inches (10 cm.) in diameter, which were most widespread on the abdomen, lower part of the back, thighs and right leg. Smaller lesions of more recent origin were present in the axillas and on some parts of the trunk. Several finger nails were pitted, and some showed circumscribed subungual scaly papules. Several toe nails were somewhat thickened and cloudy.

Treatment was started on June 14 with defatted wheat germ, 2 tablespoonfuls per day, and some of the lesions were treated with an ointment consisting of 3 per cent coal tar in a vanishing cream base. By July 11 all the lesions had cleared up, leaving pigmented patches; only on the border of several of the larger patches were a few coin-sized residual lesions. Treatment with defatted wheat germ was continued, but the residual lesions were still present. They did not yield to local therapy, general or local ultraviolet irradiation, application of tar or injections of colloidal manganese.

The examination of the blood on December 3 showed 218 mg. of cholesterol per hundred cubic centimeters. Treatment with soybean phosphatides had no effect

on the eruption. Two roentgen treatments, on Feb. 27 and March 7, 1942, produced no change in the lesions.

The eruption now consists of a few psoriatic patches scattered on the trunk and lower extremities, the largest one about the size of a quarter.

CASE 5.—R. L., a boy 7 years of age, had an eruption of psoriasis of one year's duration. He had received various local treatments, including roentgen therapy, and a tonsillectomy had been performed during the summer of 1941. There was no definite history of psoriasis in the family. His grandmother had suffered from an eruption which was found to be due to a dietary deficiency.

When he was seen on Oct. 30, 1941 the eruption consisted of erythematous patches covered with heavy micaceous scales on the scalp and inveterate plaques of psoriasis on the left elbow and both legs, covered with a thick layer of scales. Each lesion was about the size of a dollar or larger. In addition, there was a widespread eruption of guttate psoriasis on the trunk.

Treatment consisted of defatted wheat germ, 3 teaspoonfuls a day, and local therapy, oatmeal baths and an ointment containing 5 per cent salicylic acid. By November 27 the large lesions showed evidence of central healing but there were still some new lesions developing. Treatment was continued with wheat germ and a cod liver oil concentrate of low potency, 2 tablets per day. An ointment containing 3 per cent coal tar in a vanishing cream base was recommended for the lesions on the body.

By December 23 most of the lesions had completely healed but there were still a few small residual patches on the periphery of the former large plaques on the lower extremities. The eruption on the scalp had cleared up entirely. When the patient was seen on February 26, the only psoriatic lesions were a lentil-sized scaly patch on the left elbow and a small lesion on the flexor surface of each arm. The scalp, trunk and extremities were free of eruption, and the trunk showed a leukoderma psoriaticum. The patient was seen on June 4 with a mild recurrence, consisting of several lentil-sized to dime-sized patches on both elbows and one lesion on the right thigh. The scalp and the rest of the body were free of psoriasis.

CASE 6.—Miss G. McG., aged 43, was first seen on Jan. 29, 1941 at Vanderbilt Clinic. She gave a history of psoriasis of about ten years' duration, and her present attack had begun in November 1940.

She was treated with ultraviolet irradiation, viosterol in oil by mouth and injections of colloidal manganese. The eruption did not improve with this treatment. On June 10 treatment was started with soybean phosphatides, but the eruption continued to get worse.

When the patient was seen on July 30, there were numerous inveterate patches, varying in size up to that of a dollar, scattered over the entire trunk and upper and lower extremities, including the backs of the hands. There were also many new guttate lesions present. On the soles were large erythematous and hyperkeratotic plaques, which were studded with small deep-seated vesicles. There were red and scaly patches scattered throughout the entire scalp. The nails of the first and second toes of both feet showed circumscribed subungual papules. The eruption was so severe and the condition of the soles so painful that the patient was advised to move to Arizona. In an attempt to make her more comfortable, she was given 9 tablets of a yeast concentrate and later defatted wheat germ. She also received ten injections of a colloidal manganese preparation.

Because of the acute inflammation of the lesions, at first only boric acid ointment could be used. Later some of the inveterate lesions were treated with a 3 per cent

tar ointment. Four treatments with roentgen rays were applied to the soles, totaling 250 r.

The acute condition gradually quieted down, and the eruption began to improve slowly. After about four weeks of medication with defatted wheat germ the improvement was dramatic, and by October 6 the eruption on the scalp and body had completely cleared up except for small residual patches on the soles. From November 1941 until March 1942 the patient was given fifteen general body exposures to ultraviolet radiation in suberythematous doses. On account of a diffuse loss of hair due to the psoriatic eruption, local treatments with ultraviolet rays were given to the scalp. She continued taking 2 tablespoonfuls of defatted wheat germ daily throughout the winter, and she has remained entirely clear from psoriasis. She was presented before the Section of Dermatology and Syphilis of the New York Academy of Medicine on March 3, 1942.[33]

When the patient was first seen, her hair was almost completely gray. This severe graying had developed about the time of onset of the last severe attack of psoriasis. In March 1942 there had been a satisfactory regrowth of hair on the scalp and the hair had turned dark reddish brown except for a streak of gray in the midfrontal region.

When she was seen on May 8, 1942 there was no recurrence of psoriasis. The finger nails were perfect and the toe nails were normal except for slight roughness on the nails of the big toes. Her hair was dark brown and the graying streak in the center was disappearing. Only the distal portion of the hair in this streak was still gray.

Although soybean lecithin had not helped in case 6 after one month's trial, it was the effective lipotropic substance in cases 7 and 8.

CASE 7.—M. P., a woman aged 52, a factory worker, was seen on May 12, 1941. She had had psoriasis continuously for eighteen months. The patient had used only mild ointments.

On examination the trunk and extremities were covered with discoid, erythematous, lichenified and scaly plaques. In addition, on the posterior aspect of the trunk were a number of small erythematous scaly lesions. The patient was poorly nourished, and her teeth were in need of dental repair. There was nothing noteworthy in the general physical examination.

The results of some laboratory examinations were as follows: serum cholesterol content 237 mg. per hundred cubic centimeters, cephalin flocculation normal and basal metabolic rate —19 per cent.

From May 12 to November 4 the patient received 30 Gm. of soybean lecithin daily without restriction in diet and without local therapy. No new lesions appeared after the first week of therapy, and there was a slow progressive involution of all the lesions. On November 4 the peripheries of a few of the large lesions on the elbows were still visible. By December 6 all the lesions had disappeared and the patient's skin was entirely normal except for a few areas of depigmentation where lesions had been previously. The serum cholesterol on March 12, 1942, was 160 mg. per hundred cubic centimeters. The patient has continued to take from 1 to 2 Gm. of soybean lecithin daily and was free from psoriasis when last seen, on May 29, 1942.

CASE 8.—S. M., aged 54, a housewife, was first seen on May 12, 1941, with a history of psoriasis continuously for twelve years. It was gradually becoming worse

33. Gross, P., and Kesten, B.: Psoriasis Treated with Defatted Wheat Germ: Repigmentation of Grayed Hair, Arch. Dermat. & Syph. **46**:889 (Dec.) 1942.

except in the summer time. The patient had had numerous types of therapy, including tar and ultraviolet irradiation, radiotherapy and dihydroxyanthranol (anthralin), with temporary benefit but never complete clearing. The general health had always been good. The patient had a good appetite and ate moderately. Her mother died of diabetes.

On examination there were chronic discoid indurated plaques on the elbows and knees and over the lumbar vertebrae. Scattered over the extremities and trunk were guttate lesions. The scalp and nails were free. The lesions varied in size from 1 to 8 cm. in diameter. They were erythematous and covered with thick micaceous scales. Most lesions were indurated, and when the scales were removed typical bleeding points were left. There were about sixty lesions in all.

The physical examination showed no abnormalities. The patient was of normal weight for her height.

The results of laboratory examinations were as follows: urine normal, blood cell count normal, serum cholesterol 290 mg. per hundred cubic centimeters, basal metabolic rate — 22 per cent and cephalin flocculation negative.

From May 12 to October 6 the patient received 60 Gm. of soybean lecithin (oil-free phosphatides) daily without restriction in diet or local therapy. After the first month no new lesions appeared. A gradual involution of the plaques was evident by the end of the second month. The lesions healed in the center, and the scales were greatly diminished, becoming smaller and less thick. This involution continued until by the end of the fifth month the skin was entirely free of lesions. At this time the serum cholesterol content was 185 mg. per hundred cubic centimeters. The intake of soybean lecithin was reduced to 4 Gm. daily. This dose has been maintained, and the patient has remained free from lesions over an observation period of eight months.

About 40 patients with chronic psoriasis are under treatment with either the wheat germ or the soybean lecithin and with or without the addition of local therapy. In most instances within a few weeks of administration of these lipotropic substances new psoriatic patches have ceased to appear and a gradual involution of the plaques has begun. Three patients, each with an initial attack of psoriasis of less than six weeks' duration, had complete clearing in less than a month. The only therapy was administration of soybean lecithin and local application of 3 per cent colloidal tar ointment. In some cases of chronic psoriasis the condition has proved resistant to this type of therapy. Further studies are necessary to analyze the factors which may account for the lack of success in these.

COMMENT

Substances derived from natural foodstuffs have been found to have a therapeutic effect on the eruption of psoriasis. Both soybean lecithin and defatted wheat germ contain inositol. The cephalin fraction of the soybean contains from 5 to 10 per cent crude inositol and the defatted wheat germ about 0.25 per cent. It seems doubtful that the therapeutic effect is due to inositol alone. The lecithin fraction of the soybean product is also a rich source of choline (about 3 per cent), while the defatted wheat germ is poor in this substance. In contra-

distinction, the wheat germ is a well balanced vitamin B complex, containing biotin and also iron, manganese and other minerals, while these substances are lacking in the soybean phosphatides.

The question of which component or components are responsible for the lipotropic and antipsoriatic effect of soybean phosphatides and defatted wheat germ therefore cannot be answered at present. It remains to be seen whether there is a complementary action between these substances or whether there are patients who respond better to the soybean phosphatides than to defatted wheat germ and vice versa.

The average daily dose of the soybean lecithin varied between 30 and 60 Gm. With the disappearance of the lesions the patients were kept on a maintenance dose of 4 to 8 Gm. daily. The defatted wheat germ was given in doses of 30 to 45 Gm. a day, and the maintenance dose was 15 to 30 Gm. daily. Local therapy, particularly a mild tar cream, seemed to hasten the involution of the lesions. An attempt to improve simultaneously the constitutional anomalies by removal of focal infection, by rest, by psychotherapy and by nonspecific therapy and intelligent endocrine treatment may further reduce the percentage of failures. The experience of Dragstedt and his co-workers with lipocaic suggests that there will remain a group of cases of psoriasis that will present further therapeutic problems.

We present these hypothetic considerations in the hope that they will be accepted by experienced dermatologists as having ample support in a century of clinical observation. An especial reason for repeating many well known facts is a desire to be understood as presenting not a new cure of psoriasis but rather an effective remedy in the hands of dermatologists, who alone understand the problem of psoriasis.

SUMMARY AND CONCLUSIONS

A series of patients with psoriasis of varying degrees of severity was treated with lipotropic substances derived from foodstuffs with good therapeutic effect. This strengthens the opinion that psoriasis is a disturbance of lipid metabolism.

Abnormalities in the constitutional makeup are considered as the cause of this disturbance in fat metabolism, at least in the majority of cases.

The favorable response of psoriasis to lipotropic substances derived from foods reflects not a nutritional deficiency but rather an increased requirement for certain foodstuffs essential for the synthesis of enzymes engaged in lipid metabolism.

Soybean lecithin and VioBin (defatted wheat germ) were effective in reducing an elevated serum cholesterol content in 5 patients.

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DOUBTFUL VALUE OF SODIUM THIOSULFATE IN THERAPY OF ARSENICAL DERMATITIS

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For almost two decades sodium thiosulfate has been accepted as the drug of choice in the treatment of arsenical dermatitis. Although dissenting opinion has existed throughout this period, it has never achieved widespread attention. More recently, however, the literature has emphasized the scarcity of evidence favoring the use of this drug. Chargin,[1] in particular, has voiced the doubt of an important group of dermatologists as to the value of sodium thiosulfate for any of the manifestations of arsphenamine toxicity.

One of the reasons given for thinking that sodium thiosulfate is beneficial in arsenic poisoning is based on Osborne's studies [2] of the behavior of certain crystals in the skin which he believed to be arsenic trisulfide. Montgomery and Waisman [3] stated the belief that their investigations confirmed Osborne's findings. These crystals have been noted by others [4] in the tissues both of normal persons and of persons

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1. Chargin, L.: Massive Arsenotherapy in Early Syphilis by the Continuous Intravenous Drip Method: Toxicologic Manifestations, Arch. Dermat. & Syph. **42**: 248 (Aug.) 1940.

2. (*a*) Osborne, E. D.: Microchemical Studies of Arsenic in Arsenical Pigmentation and Keratoses, Arch. Dermat. & Syph. **12**:773 (Dec.) 1925; (*b*) Microchemical Studies of Arsenic in Arsenical Dermatitis, ibid. **18**:37 (July) 1928. (*c*) Osborne, E. D.; Putnam, E. D., and Hitchcock, B. S.: The Effect of Arsenic in Rabbits: Microchemical Studies Following the Administration of the Arsphenamines and Tryparsamide, ibid. **25**:419 (March) 1932.

3. Montgomery, H., and Waisman, M.: Epithelioma Attributable to Arsenic, J. Invest. Dermat. **4**:365 (Oct.) 1941.

4. (*a*) Tannenholz, H., and Muir, K. B.: Methods for Microchemical Demonstration of Arsenic in Tissues, Arch. Path. **15**:789 (June) 1933. (*b*) Oppenheim, M., and Fantl, P.: Personal communication to M. R. Mattice, 1937; Das Natriumthiosulfat in der Behandlung von durch Arsenverbindungen verursachten Hauterkrankungen, Arch. f. Dermat. u. Syph. **175**:438, 1937; Ueber Hauterkrankungen verursacht durch arsenhaltige Wandfarben: II. Versuche zum histologischen Nachweis von Arsenverbindungen in der Haut, ibid. **170**:488, 1934.

with arsenical dermatitis, but the proof offered for their chemical composition by Osborne has been questioned. Since the identity of the crystals is in doubt, it is futile to present them as evidence for the efficacy of treatment with sodium thiosulfate. This is not to say that arsenic does not exist in tissues; it is deposited in various parts of the body in amounts depending on exposure to the element and on speed of excretion. Magnuson and Raulston [5] in histologic studies of dogs undergoing intensive treatment with neoarsphenamine and mapharsen did not mention the crystals described by Osborne.

Since the chief route for elimination of arsenic from the body is through the biliary tract, it has often been taken for granted that sodium thiosulfate would aid this excretory process. Some evidence supporting this view is found in the work of Appel and Jankelson,[6] but it should be noted that they administered neoarsphenamine and sodium thiosulfate simultaneously to rabbits, killed the animals within twenty-four hours and then analyzed the liver and bile for arsenic. These investigators, however, obtained better results with sodium dehydrocholate. The question of the effect of sodium thiosulfate on excretion of arsenic through the bile has been thoroughly examined recently by Ceder, Zon and Klinger,[7] and they have demonstrated in human subjects after completion of a course of neoarsphenamine therapy that sodium thiosulfate does not significantly affect the urinary or fecal arsenic output.

The most recent investigation [8] upholding therapy with sodium thiosulfate was based on a method of collecting urine which, in our opinion, is apt to give misleading results. This is the only favorable report which has come to our attention in over five years.

MATERIAL AND METHODS

The cases we have to report are typical of those commonly designated as instances of arsenical dermatitis. Several cases of dermatitis due to bismuth and gold are included. Not all patients are suitable for study, because of failure to cooperate. The securing of data on which

5. Magnuson, H. J., and Raulston, B. O.: The Concentration of Arsenic in Tissues and the Excretion of Arsenic by Experimental Animals Following Intravenous Injection of Massive Doses of Mapharsen, Ann. Int. Med. **14**:2199 (June) 1941.

6. Appel, B., and Jankelson, I. R.: Treatment of Arsenical Hepatitis with Sodium Dehydrocholate, Arch. Dermat. & Syph. **32**:422 (Sept.) 1935.

7. Ceder, E. T.; Zon, L., and Klinger, M. E.: Effect of Sodium Thiosulfate on Excretion of Arsenic, Ven. Dis. Inform. **22**:123 (April) 1941.

8. Ayres, S., Jr., and Anderson, N. P.: Sodium Thiosulfate and the Elimination of Arsenic, J. A. M. A. **110**:886 (March 19) 1938.

to base conclusions as to the merits of treatment with sodium thiosulfate usually means hospitalization of the patient and laboratory work more than routine in nature.

The same diet was not employed for all patients reported on, but adaptations were made according to circumstances. When possible, the patient was given the banana and milk diet of Mattice and Harrison.[9] The diet described as "restricted" is that of Mattice and Weisman.[10]

Determinations of arsenic were made as previously described,[10] but attention should be called to one point. Some investigators[7] have failed to obtain satisfactory results with an electrolytic Gutzeit procedure. This is true in our experience if the amount of arsenic in the testing apparatus exceeds 5 micrograms. The best results are secured when the sample contains 2 to 3 micrograms of arsenic as arsenic trioxide. We have not relied on individual determinations of arsenic, since it is none too easy to control or predict the urinary output of normal persons, let alone that of persons who are ill. Whenever possible, a control period of three days has been followed by three days for sodium thiosulfate therapy and then three days for after-effects.

One gram of sterilized crystalline sodium thiosulfate freshly dissolved in 10 cc. of sterile water was administered intravenously. A recent communication[11] notes the possibility of administering the wrong substance. Adherence to standard terminology would obviate any possible error. Although there can be no doubt as to the identity of sodium thiosulfate, this is not true when the product is labelled "hyposulfite." Three different compounds ($Na_2S_2O_3$, $Na_2S_2O_4$ and $NaHSO_2$) have been called sodium hyposulfite. Officially[12] the respective names are sodium thiosulfate, sodium dithionite and sodium sulfoxylate. Hydrosulfite is a term frequently applied to $Na_2S_2O_4$. "Hyposulfite" should be discarded or relegated to technical grades of sodium thiosulfate,

9. Bridges, M. A.: Dietetics for the Clinician, ed. 4, Philadelphia, Lea & Febiger, 1941, p. 502.

10. Mattice, M. R., and Weisman, D.: (*a*) Urinary Excretion of Arsenic: I. Normal Subjects, Am. J. M. Sc. **193**:413 (March) 1937; II. The Influence of Thiosulfate, ibid. **193**:420 (March) 1937. (*b*) Mattice, M. R.; Baxt, H., and Byrne, J. M.: Effect of Thiosulfate on Arsenic Excretion, Arch. Dermat. & Syph. **42**:399 (Sept.) 1940.

11. Muir, K. B.; Stenhouse, E., and Becker, S. W.: Action of Sulfur-Containing Compounds in Arsenical and Mercurial Poisoning, Arch. Dermat. & Syph. **41**:308 (Feb.) 1940.

12. Jorissen, W. P.; Bassett, H.; Damiens, A.; Fichter, F., and Remy, H.: Rules for Naming Inorganic Compounds: Report of the Committee of the International Union of Chemistry for the Reform of Inorganic Nomenclature, 1940, J. Am. Chem. Soc. **63**:889 (April) 1941.

although "hypo" may still be retained as the photographer's designation for sodium thiosulfate without confusion. It should be noted in passing that Bond and Gray [13] used sodium hydrosulfite with success in the oral treatment of acute poisoning due to experimental administration of potassium arsenite. Earlier Haag and Bond [14] found sodium thiosulfate of no value under such circumstances.

REPORT OF CASES

CASE 1.—L. B. R., a white man 51 years old, with meningovascular syphilis, received thirty-three injections of bismuth subsalicylate in oil, thirty-one of silver arsphenamine and sixteen of sodium thiosulfate and three spinal fluid drainages from Oct. 17, 1938 to Dec. 29, 1939. He was given ten injections of silver arsphenamine and four of sodium thiosulfate and 1 spinal fluid drainage from Jan. 15, 1940 to April 5, 1940. Following the last injection of silver arsphenamine on April 5, a generalized patchy subacute eczematous eruption was noted on his body and extremities. The patient was admitted to the New York Post-Graduate Medical School and Hospital

TABLE 1.—*Results of Determinations of Arsenic in Case 1*

Date, 1940	Urine Volume, Cc.	Arsenic as As_2O_3, Mg./Vol.	Comment
5/1	1,400	0.14	Restricted diet; breadstuffs
5/2	2,145	Approx. 0.10	allowed
5/3	1,645	0.32	
5/5	880	0.09	1 Gm. sodium thiosulfate
5/6	910	Approx. 0.05	1 Gm. sodium thiosulfate
5/7	980	0.39	1 Gm. soduim thiosulfate
5/8	825	Approx. 0.07	

(service of Dr. I. Rosen), where the arsenic studies were made. While the patient was hospitalized the eruption improved slowly. It did not clear up completely until four months later.

CASE 2.—E. B. A., a 54 year old man with asymptomatic neurosyphilis, received irregular treatment from 1918 to 1939. In 1939 he received twenty injections of bismuth subsalicylate in oil and ten injections of neoarsphenamine. After the last injection of neoarsphenamine, in October 1939, a patchy generalized erythematous scaly eruption developed on the body, which persisted until Feb. 12, 1940, when he was admitted to the New York Post-Graduate Medical School and Hospital (service of Dr. I. Rosen). The patient received an undetermined number of injections of bismuth subsalicylate in oil and of liver extract from the date of onset of the eruption to the date of his admission to the hospital. The eruption improved about 50 per cent while the patient was hospitalized. Patch tests with graded dilutions of tryparsamide, neoarsphenamine and bismuth subsalicylate in oil gave negative results. Arsenic could not be detected in a specimen of skin taken for biopsy and reported as showing

13. Bond, W. R., and Gray, E. W.: Sodium Hydrosulphite in Treatment of Acute Arsenical Poisoning, J. A. M. A. **92**:1919 (June 8) 1929.

14. Haag, H. B., and Bond, W. R.: Value of Sodium Thiosulphate in Poisoning from Oral Administration of Arsenic, J. A. M. A. **88**:1219 (April 16) 1927.

arsenical dermatitis at the Skin and Cancer Unit of the aforementioned hospital. The patient was also hospitalized from March 7 to 13, 1940 for further studies with regard to arsenic. The eruption completely subsided by April 1, 1940.

CASE 3.—F. M. C., a 35 year old Negro with latent syphilis, received alternating courses of bismuth subsalicylate in oil and neoarsphenamine from June 1, 1939 to June 3, 1940. He was given 0.3 Gm. of neoarsphenamine on May 20, 0.45 Gm. on May 27 and 0.60 Gm. on June 3. A day after the last injection he noted a

TABLE 2.—*Results of Determinations of Arsenic in Case 2*

Date, 1940	Urine Volume, Cc.	Arsenic as As_2O_3, Mg./Vol.	Comment
2/ 2	695	0.14	Diet: bananas and milk, coffee (no sugar); smoked a pipe; used no lotions; allowed talcum powder and starch bath
2/ 3	1,640	0.16	
2/ 4	1,720	0.51	
2/ 5	1,420	0.14	
2/ 6	1,660	0.08	1 Gm. sodium thiosulfate
2/ 7	1,370	0.11	1 Gm. sodium thiosulfate
2/ 8	1,445	<0.10	1 Gm. sodium thiosulfate
2/ 9	1,910	0.10	
2/10	1,290	0.15	
2/11	2,010	0.08	
3/ 7	1,360	0.14	
3/ 8	1,960	<0.10	
3/ 9	1,810	<0.10	2 Gm. sodium thiosulfate
3/10	1,620	<0.10	2 Gm. sodium thiosulfate
3/11	1,290	0.12	
3/12	1,220	<0.10	

TABLE 3.—*Results of Determinations of Arsenic in Case 3*

Date, 1940	Urine Volume, Cc.	Arsenic as As_2O_3, Mg./Vol.	Comment
6/12	3,910	0.62	Regular diet
6/13	2,790	0.56	Banana and milk diet
6/14	3,220	0.96	
6/16	1,660	0.67	
6/17	1,405	0.56	1 Gm. sodium thiosulfate; 6 slices of bread and 6 squares of butter added to daily diet
6/18	720	0.36	1 Gm. sodium thiosulfate

patchy generalized erythematosquamous eruption on his body, face and extremities. The patient was admitted to Bellevue Hospital (service of Dr. E. Thomas) on June 12 and given an arsenic-free diet and injections of sodium thiosulfate. Because his condition became worse the patient refused to cooperate, and the studies were discontinued.

CASE 4.—B. F. A., a 25 year old white man, was admitted to Bellevue Hospital (service of Dr. E. Thomas) on May 31, 1940 with a generalized exfoliative erythroderma. He had received two injections weekly of 0.3 Gm. of neoarsphenamine for five weeks because of a seropositive primary lesion in the perineal region. He received the last injection on May 24. Despite the arsenic-free diet and the use of sodium thiosulfate his condition became much worse, and he died on June 15.

Case 5.—E. S. H., a 41 year old white man, was admitted to the New York Post-Graduate Medical School and Hospital (service of Dr. Fred Wise) on Oct. 14, 1940, with a generalized exfoliative erythroderma involving the entire body but most severe in the flexural regions and on the soles. There was hyperpigmentation of the flexural areas. Beginning in March 1940, he received two series of twelve intravenous injections of 0.45 Gm. of neoarsphenamine and two series of fifteen intramuscular injections of bismuth subsalicylate in oil. The injections were given twice weekly. During hospitalization the eruption improved slowly. When the patient was examined two months after he had left the hospital, the eruption was still present but improved about 70 per cent.

Table 4.—*Results of Determinations of Arsenic in Case 4*

Date, 1940	Urine Volume, Cc.	Arsenic as As_2O_3, Mg./Vol.	Comment
6/ 1	2,080	17.2	Restricted diet
6/ 2	2,420	18.2	
6/ 3	1,890	11.3	1 Gm. sodium thiosulfate
6/ 4	3,840	7.7	1 Gm. sodium thiosulfate
6/ 5	2,880	6.8	1 Gm. sodium thiosulfate
6/12	1,540	7.7	
6/13	820	3.4	
6/15	450	0.9	Died

Table 5.—*Results of Determinations of Arsenic in Case 5*

Date, 1940	Urine Volume, Cc.	Arsenic as As_2O_3, Mg./Vol.	Bismuth as Bi, Mg./Vol.	Comment
10/14	720	0.25	0.29	Diet: cottage cheese, bananas,
10/15	610	0.24	0.23	milk, cream, butter, 2 slices
10/17	1,295	0.39	0.52	white bread daily
10/18	485	0.19	0.05	1 Gm. sodium thiosulfate
10/19	645	0.06	0.05	1 Gm. sodium thiosulfate
10/20	890	0.09	0.18	1 Gm. sodium thiosulfate
10/21	1,080	0.20	0.20	
10/22	1,250	0.25	0.50	

It is interesting to note that the bismuth excretion appears to have been adversely affected by the sodium thiosulfate, although the small output of water on the test days may have been responsible for the findings. Subsequent tests on excretion of bismuth (October 31 to November 14) were unsatisfactory because of the low concentration encountered. The method used was that of Hanzlik and co-workers [15] except that standard solutions of bismuth were used for comparison.

Case 6.—C. M. U., a white woman aged 50, with early tabes dorsalis and aortitis attended a New York City Department of Health Clinic from Oct. 10, 1939 to Nov. 15, 1940. She received thirty-one injections of a bismuth compound, five of neoarsphenamine and seven of mapharsen. She was seen at the New York Skin and Cancer Hospital on Nov. 19, 1940, suffering from a generalized arsenical

15. Hanzlik, P. J.; Lehman, J. A.; Richardson, A. P., and Van Winkle, W., Jr.: Rapid Clinical Method for Estimation of Bismuth in Urine, Arch. Dermat. & Syph. **36**:725 (Oct.) 1937.

dermatitis which she stated had been present from the middle of October 1940. She was admitted to the New York Post-Graduate Medical School and Hospital (service of Dr. I. Rosen) on December 12 for studies of urinary excretion of arsenic. The eruption improved slowly but was still present two months after the patient left the hospital.

The excretion of bismuth showed no consistent variation following sodium thiosulfate therapy, but elimination of this metal certainly was not stimulated.

CASE 7.—D. C., a white woman aged 48, received weekly intramuscular injections of aurothiodextrose (solganol B) from Sept. 30, 1941 to December 11 (total gold 370 mg.) for rheumatic arthritis of the hands. Five days (December 16) after

TABLE 6.—*Results of Determinations of Arsenic and Bismuth in Case 6*

Date, 1940	Urine Volume, Cc.	Arsenic as As_2O_3, Mg./Vol.	Bismuth as Bi, Mg./Vol.	Comment
12/10	295	<0.10	0.90	Diet: bananas, cream, milk, cottage cheese, 6 slices whole wheat bread, 6 squares butter daily
12/11	1,620	Approx. 0.10	1.30	
12/12	1,660	Approx. 0.10	1.00	
12/13	1,680	<0.10	0.67	1 Gm. sodium thiosulfate
12/14	1,720	<0.10	0.52	1 Gm. sodium thiosulfate
12/15	1,010	<0.10	0.81	1 Gm. sodium thiosulfate
12/16	1,260	Approx. 0.10	0.50	
12/17	1,800	<0.10	0.54	

TABLE 7.—*Results of Determinations of Gold in Case 7*

Date, 1942	Urine Volume, Cc.	Gold as Au, Mg./Vol.	Comment
2/27	1,070	0.06	Regular ward diet
2/28	300	0.06	
3/ 1	1,150	0.10	
3/ 2	900	0.07	1 Gm. sodium thiosulfate
3/ 3	725	0.08	1 Gm. sodium thiosulfate
3/ 4	970	0.06	1 Gm. sodium thiosulfate
3/ 5	850	0.08	
3/ 6	400	0.05	
3/ 7	610	0.07	

the last injection she began to complain of sore throat. An itchy eruption of the body is said to have appeared at the end of December. She was admitted to the New York Post-Graduate Medical School and Hospital on Feb. 21, 1942 (medical service of Dr. Joseph Eidelsberg). The mucous membrane of the cheeks presented pearly white fine mesh areas as seen in lichen planus. The trunk was covered with oval, almond-sized, scaly papular lesions with pigmentation. The biopsy revealed lichen planus of the skin.

The excretion of gold on the average was about the same or slightly less during and after sodium thiosulfate therapy. The smaller output of water in the test may account for these findings. Some improvement in the eruption followed this therapy.

COMMENT

The availability of arsenic for urinary excretion is reflected in the findings in the various cases. When the injection of arsphenamine is

recent, as in case 4 (a week previous), relatively large amounts of arsenic are excreted. The sodium thiosulfate, if anything, suppresses the diminishing arsenic concentration. In case 3, nine days after arsphenamine was given, much less was eliminated than in case 4. Since the sodium thiosulfate was of no apparent clinical benefit to the patient and did not aid in the urinary excretion of arsenic, its administration was discontinued. The findings in case 6 are precisely those of normal persons on the same routine; the arsenic content of the urine gives no clue to the cause of the dermatitis—unfortunately, this must be supplied by the patient's history and the clinical picture. Our studies give no indication that sodium thiosulfate is of value in the elimination of arsenic via the urinary tract.

One of the reasons for the difference in opinion as to the effect of sodium thiosulfate on the urinary excretion of arsenic has been the manner of expressing results. It has been suggested to us that our data should be calculated otherwise. If the urine volume and arsenic output shown in table 1 are added together, it will be seen that 0.56 mg. was eliminated in 5,190 cc. of urine prior to the administration of sodium thiosulfate and 0.53 mg. in 2,770 cc. during therapy. Expressed on a per liter basis, the output was 0.11 mg. before ($0.56 \times 1{,}000 \div 5{,}190$) and 0.19 mg. ($0.53 \times 1{,}000 \div 2{,}770$) during therapy. The conclusion from these figures is that sodium thiosulfate aids in the elimination of arsenic. As we have presented the data, the average daily output of arsenic on the three days prior to the giving of the drug was just less than 0.19 mg. The average daily output during therapy was almost 0.18 mg. If the amount on the last day is included, this average falls to 0.15 mg. From these data, it is apparent that there was a decrease of arsenic excretion, although the change is not statistically significant. What then is to be the criterion of arsenic excretion: the concentration or the twenty-four hour output?

In papers dealing with the sodium thiosulfate problem, concentration of arsenic has been expressed in terms of water output (as milligrams per liter) or in terms of solid waste (as milligrams per hundred grams of dried urine).[16] Is not the amount eliminated in twenty-four hours the best clinical guide? It is the observation of one of us (M. R. M.) that the total daily output of arsenic does not rise and fall with ordinary variation in urine volume in normal persons. As in the case under discussion, a drop in volume is accompanied by a rise in concentration, to the end that the amount of arsenic eliminated is about the same regardless of the changes in water.

16. Myers, C. N.; Groehl, M. R., and Metz, G. P.: (*a*) Therapeutic Activity of Sodium Thiosulfate, Proc. Soc. Exper. Biol. & Med. **23**:97, 1925. (*b*) Myers, C. N.; Marples, E.; Groehl, M. R., and Throne, B.: The Use of Sodium Thiosulfate in Diagnostic Procedures, J. Lab. & Clin. Med. **11**:836, 1926. (*c*) Ayres and Anderson.[8]

Webster [17] has noted the tendency for high concentrations of arsenic and other metallic elements to be associated with low urinary volumes, and he stated: "The assumption that identical concentrations signify approximately equal outputs is clearly unwarranted." He also has observed that values for urinary arsenic are subject to considerable fluctuation and that fractional day samples give little information regarding the daily output. The total twenty-four hour output would seem to be the logical criterion of arsenic elimination.

The augmented excretion of arsenic assumed to occur with sodium thiosulfate therapy has been attributed to diuresis. Although there is a general impression among clinicians that this drug acts as a diuretic, we have never observed such an effect; the output of water has depended on the intake.

Injections of arsenicals lead to decided and prompt urinary excretion. After these are discontinued, the concentration falls rapidly and within five to seven days reaches a low level. All too frequently patients present themselves at the dermatologic clinic some weeks after the injection of the offending arsenical. The urinary and fecal excretion then largely represent intake through dietary channels or cutaneous applications. The arsenic which fails to be excreted promptly is later removed at a level which cannot be distinguished from the outpouring of arsenic through the kidneys and thus alleviates the cutaneous complaints. Conversely, the finding of a high urinary concentration of arsenic after injection of sodium thiosulfate has been taken to indicate that a presenting dermatologic lesion is of arsenical causation. Unfortunately, these hopes have not been realized.

Whenever the output of arsenic is small, the dietary intake may introduce a variable of sufficient importance to give misleading results. Normal persons on ordinary diets may excrete over 1 mg. of arsenic (as arsenic trioxide) per day, although the amount usually is about one third of this.[10] If it can be taken for granted that the intake over two to three days is negligible, then it may be permissible to assume that the urinary excretion of more than 0.1 mg. of arsenic trioxide per day indicates the removal of stored arsenic. However, elimination of stored arsenic may be so slow as to defy ready detection. There is no guarantee that the stored element will be extracted from the tissues by the simple expedient of diminishing dietary intake. There are still undetermined factors in the excretion of arsenic which complicate the problem.

CONCLUSIONS

1. Using as a criterion the twenty-four hour output of arsenic, we have been unable to demonstrate that sodium thiosulfate in the doses

17. Webster, S. H.: Twenty-Four Hour Output of Certain Urinary Constituents in Persons Exposed to Lead Arsenate Spray Residue, Pub. Health Rep. 56:1910 (Sept. 26) 1941.

commonly employed increases the urinary secretion or alleviates dermatitis due to the arsphenamines. It is therefore of little diagnostic or therapeutic value.

2. Although our experimental evidence is limited, it would appear that sodium thiosulfate is without effect on urinary excretion of bismuth or on dermatoses subsequent to alternate bismuth and arsenic therapy. In 1 case the urinary excretion of gold also was not affected by sodium thiosulfate.

NOTE.—After the article was submitted for publication the following case was observed.

CASE 8.—C. K., a 33 year old white man, was admitted to the New York Post-Graduate Medical School and Hospital (service of Dr. I. Rosen) on July 29, 1942.

TABLE 8.—*Results of Determinations of Arsenic in Case 8*

Date, 1942	Urine Volume, Cc.	Arsenic as As_2O_3, Mg./100 Cc.	Arsenic as As_2O_3, Mg./Vol.	Comment
8/ 5	1,710	0.20	3.42	Fly in specimen
8/ 6	1,880	0.09	1.69	
8/ 7	495 ?	0.08	0.40	
8/ 8	1,830	0.08	1.46	
8/ 9	1,310	0.06	0.78	
8/10	765	0.10	0.76	
8/11	385 ?	0.12	0.46	
8/12	2,135	0.07	1.49	
8/13	845	0.04	0.34	
8/14	1,480	0.04	0.59	
8/15	965	0.03	0.29	
8/16	1,290	0.05	0.64	
8/17	990	0.05	0.50	
8/18	1,780	0.04	0.71	
8/19	1,755	0.04	0.70	

He had a generalized pigmentation of the trunk and extremities and scattered circular depigmented areas, all of two years' duration. These affected areas were the sites of former lesions of dermatitis herpetiformis. The palms, sides of the fingers and soles showed typical arsenical keratoses. The legs presented palm-sized ulcerations, also of two years' duration. Ever since the spring of 1939 the patient had been in the habit of taking 10 drops of solution of potassium arsenite U. S. P. by mouth three times a day, with practically no let-up. This apparently had a favorable influence on the dermititis herpetiformis. When he was admitted to the hospital, the values for arsenic, as arsenic trioxide, were 0.05 mg. per hundred cubic centimeters of blood and 0.01 mg. per hundred cubic centimeters of spinal fluid.

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EPITHELIAL CYSTS

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The object of this paper is to distinguish epithelial cysts from sebaceous cysts and to study the incidence of malignant change in these cysts.

This study is based on a review of the records of 271 cases of sebaceous and epithelial cysts which were excised at the Mayo Clinic during 1939 and 1940. In all cases microscopic diagnosis of sebaceous or epithelial cyst (keratoma) had been made, but not always was sharp distinction between the two types made. Of the 271 cases, in only 88 were specimens available for further study, but we believe that these cases probably represented all that were of pathologic interest.

There are relatively few articles in the literature identifying epithelial cysts, which have also been referred to as epidermoids and have been included under the broad term of atheroma. The latter term apparently has been used for both epithelial and sebaceous cysts. As early as 1853 Cock [1] described a peculiar disease of the hair follicles and distinguished it from cancer. Paget [2] described cuticular proliferous cysts tending toward hereditary origin, a few of which showed a slender cord traceable from the cyst to the skin and formed of the obliterated duct of an obstructed hair follicle. Wernher [3] observed some atheromas which had an external wall of connective tissue with an internal wall and cyst contents composed of collections of laminated epidermal tissue. Broders

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Abridgment, with additions, of a thesis submitted by Dr. Love to the faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Dermatology and Syphilology.

1. Cock, E.: A Few Remarks on a Peculiar Follicular Disease, M. Times & Gaz. **6**:159, 1853.

2. Paget, J.: Lectures on Surgical Pathology, ed. 3, Philadelphia, Lindsay & Blakiston Company, 1865, pp. 391-395.

3. Wernher, A.: Das Atherom, ein eingebalgtes Epitheliom, Arch. f. path. Anat. u. Physiol. **8**:221-248, 1855.

and Wilson [4] in 1930 definitely distinguished sebaceous cyst from epithelial cyst and called the latter keratoma because of the keratin content. Textbooks on dermatology and cutaneous neoplasms, however, use the term epithelial or epidermal cyst rather than keratoma, and this would seem to be a more specific term.

Epithelial cysts occur as slow-growing, smooth or slightly elevated, firm tumors 0.2 to 5 cm. in diameter. They are not painful or tender and do not tend to ulcerate. These cysts are usually freely movable with the skin and occur most commonly on the scalp and face and next frequently on the genitalia, trunk and extremities, in the order named. The great majority are found on the scalp. A very few are found distal to the knees. The cysts may be solitary or multiple, usually less than ten being present. They are most often of several years' duration. They are relatively uncommon in the first and second decades of life but become more frequent in middle age. There is commonly an absence of any orifice or direct connection with the cutaneous surface, in contradistinction to sebaceous cysts, for which orifices often can be demonstrated. Sebaceous cysts are usually softer than epithelial cysts, but clinical distinction between the two is not always possible. Fifty-one of the 88 specimens studied proved histologically to be epithelial cysts and confirmed the concept of Broders and Wilson that many lesions diagnosed clinically as sebaceous cysts or wens prove on microscopic examination to be epithelial cysts (keratomas).

On gross examination of an epithelial cyst one is impressed with the relative firmness, the smooth, pearly, glistening surface, absence of greasiness to the examining finger and the lack of the rancid sebaceous odor that is characteristic of sebaceous cysts when they are incised. Epithelial cysts are odorless unless infected or degenerated. When burned they give off an odor comparable to that of burning hair, wool or feathers. The cysts usually sink when an attempt is made to float them in water. They are readily sectioned, revealing a pearly and centrally laminated surface. The wall of the cyst shows a complete cycle of keratinization (fig. 1). There are usually definite papillary bodies (fig. 2) and rete ridges, which as a rule are not seen in sebaceous cysts. There are increase of the granular layer and decided production of stratum corneum, the keratinized cells of which fill the cyst in laminated layers, simulating epithelial pearls. Staining for fat with sudan III usually shows an absence of fatty material, but fatty globules and crystals of cholesterol often are seen in the center of the cyst and occasionally are associated with deposits of calcium. These crystals of cholesterol

4. Broders, A. C., and Wilson, E.: Keratoma: A Lesion Often Mistaken for Sebaceous Cyst, S. Clin. North America **10**:127-130 (Feb.) 1930.

may be the result of degeneration or may be a factor in the primary cause of keratinization.[5] There may be increased pigment in the basal cells of the outer wall of the cyst and increased fibrous tissue about the cyst. Usually there is little inflammatory reaction about the walls of a cyst, in contrast to traumatic epithelial cysts and cysts arising in relation to ingrowing hairs, where considerable infiltrate is often found.

Broders and Wilson expressed the belief that a keratoma (epithelial cyst) arises from the duct of a sebaceous gland and pointed out that

Fig. 1.—Epithelial cyst, showing (*x*) cutaneous surface, (*y*) wall of the cyst and complete cycle of keratinization and cyst filled with keratin (× 100).

the sebaceous ducts are composed of stratified squamous epithelium which differentiates into keratin, whereas in the sebaceous gland proper the epithelium divides into sebaceous cells containing droplets of fat. Most authors explain the formation of epithelial cysts as the result of obstruction of the duct following hyperkeratosis and accumulation of keratinous material which distends the walls of the duct. This continues until the nutrition of the cells is interfered with, at which stage

5. Jones, K. K.: Personal communication to the authors.

the process tends to arrest itself. Gans [6] pointed out that epithelial cysts tend to develop in the later decades of life, when activity of the sebaceous glands is diminished, and suggested that the sebaceous duct and orifice of the hair follicle tend to revert toward making stratified epidermis.

Franke [7] and Török [8] suggested that the origin of the epithelial cysts is in the ectoderm as new growths of embryonic inclusion cysts and

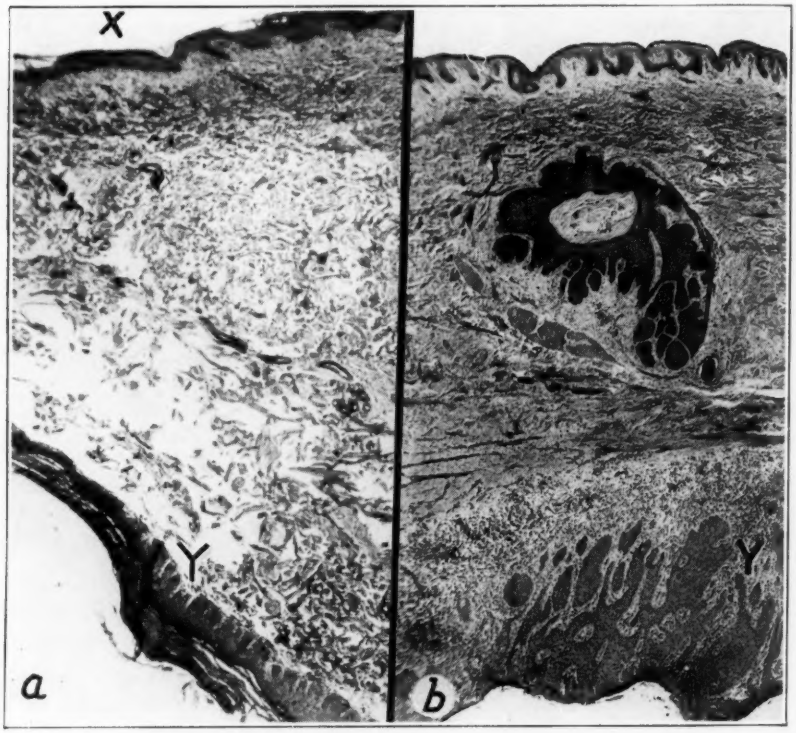

Fig. 2.—Epithelial cyst, showing in *a* (*x*) the cutaneous surface and (*y*) formation of papillary bodies in the wall (× 42) and in *b* the wall, with pseudo-epitheliomatous hyperplasia at *y* (× 22).

pointed to the presence of papillae as evidence against a hypothesis of retention. Others have stated that an epithelial cyst is a new growth

6. Gans, O.: Histologie der Hautkrankheiten: Die Gewebsveränderungen in der kranken Haut unter Berücks ihrer Entstehung und ihres Ablaufs, Berlin, Julius Springer, 1928, pp. 215-219.

7. Franke, F.: Dermoid oder Epidermoid? Wien. klin. Wchnschr. **3**:696-697 (Sept.) 1890.

8. Török, L.: Ueber die Entstehung der Atheromcysten (Epidermoide Franke) nebst einigen Bemerkungen über Follikularcysten und Doppelkomedonen, Monatsh. f. prakt. Dermat. **12**:437-450 (May); 482-492 (June) 1891.

arising by accumulation of secretion from isolated rudimentary rests of epidermal cells lying in the corium. McDonagh [9] especially referred to rudimentary cell rests in mammals about the nasolabial and anogenital folds and the role they play in regard to benign epithelioma, including epithelioma adenoides cysticum, syringoma and even epidermoids and dermoids. The concept of origin of epithelial cysts from rudimentary rests is supported (1) by the infrequency of demonstrating by serial section any occluded or obliterated duct connecting the epithelial cyst with the external surface; (2) by the presence of cysts on the palms and the volar surfaces of the fingers, which areas are normally devoid of sebaceous ducts and hair follicles; (3) by the rarity of formation of epithelial cysts in cases of severe acne; (4) by evidence that implanted full thickness skin grafts may attempt formation of epithelial cysts, and (5) by similarity of behavior of epithelial cysts and epidermoids. However, only a few of the cysts in this study were studied by serial sections, and it is quite possible that ducts connecting the cysts with the external surface could be demonstrated in some cases if further sections had been cut and wax reconstructions made.

TRAUMATIC EPITHELIAL CYSTS

Traumatic epithelial cysts were encountered in 2 of the 271 cases of sebaceous and epithelial cysts. This type (fig. 3) usually is described as developing shortly after trauma or injury and appears as a subcutaneous, hard, round cystic tumor of variable size occurring most often on a palmar or plantar surface.[10] A few cysts have been found within bony structures,[11] 6 cases having been reported in which cysts were present in phalanges. The histologic structure is that of an epithelial cyst, often associated with varying degrees of inflammatory change, including at times a foreign body giant cell reaction. Wein and Caro [12] reported 3 cases of traumatic epithelial cysts. They attributed the origin of the cysts to bits of epidermis which had been torn from the surface and implanted in the corium. The cysts also may originate in deeper epithelial structures or be the result of invaginated hairs in the presence of injury or repeated trauma. Peer [13] and Peer

9. McDonagh, J. E. R.: A Classification and Description of the Cutaneous Epitheliomata, J. Cutan. Dis. **32**:11-17 (Jan.) 1914.

10. Garrè, C.: Ueber traumatische Epithelcysten der Finger, Beitr. z. klin. Chir. **11**:524-533, 1894.

11. Yachnin, S. C., and Summerill, F.: Traumatic Implantation of Epithelial Cyst in a Phalanx, J. A. M. A. **116**:1215-1218 (March 22) 1941.

12. Wein, M. S., and Caro, M. R.: Traumatic Epithelial Cysts of the Skin, J. A. M. A. **102**:197-199 (Jan. 20) 1934.

13. Peer, L. A.: Fate of Buried Skin Grafts in Man, Arch. Surg. **39**:131-144 (July) 1939.

and Paddock,[14] however, in a study of the fate of buried skin grafts in man questioned that there was any tendency of the buried grafts to form cysts.

DIFFERENTIAL DIAGNOSIS

Milia present a histologic structure similar to that of epithelial cysts and are retention cysts with laminated horny keratinized contents (fig. 4 *a*). They are readily distinguished clinically from epithelial cysts by

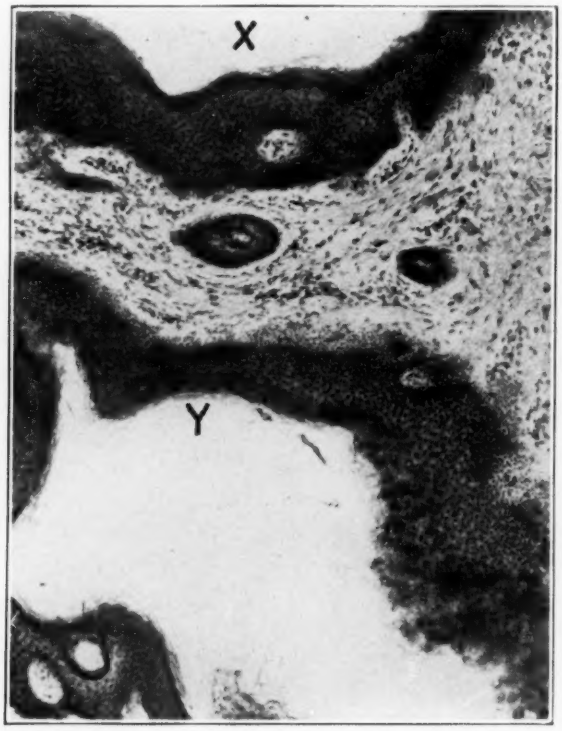

Fig. 3.—Traumatic epithelial cyst of two weeks' duration; *x* indicates the cutaneous surface and *y* the cavity of the cyst. No connection is demonstrated with epidermis in serial sections (× 80).

their multiplicity and their much smaller size. There is also a primary type known as milium congenitale.[15] Most investigators have found that horny cysts of milia develop in relation to the lanugo hair follicles, although some state that they originate in sebaceous ducts.

14. Peer, L. A., and Paddock, R.: Histologic Studies on the Fate of Deeply Implanted Dermal Grafts: Observations on Sections of Implants Buried from One Week to One Year, Arch. Surg. **34**:268-290 (Feb.) 1937.

15. Ormsby, O. S.: A Practical Treatise on Diseases of the Skin for the Use of Students and Practitioners, ed. 5, Philadelphia, Lea & Febiger, 1937, p. 1173.

Distinction of epithelial cysts from epithelioma adenoides cysticum, various types of sebaceous adenoma, naevus sebaceus, epidermoids, dermoids,[16] other benign epithelial neoplasms and hydrocystoma usually can be made by concomitant findings and especially by their different histologic pictures.[17]

Sebaceous cysts, with which epithelial cysts have long been confused, are usually softer in consistency than the epithelial cysts, being semi-fluctuant and having a rancid, foul sebaceous odor when punctured. They may occur anywhere on the body, including the locations mentioned for epithelial cysts. The sebaceous cysts when removed tend to float in water. They are filled with sebaceous cells and debris and

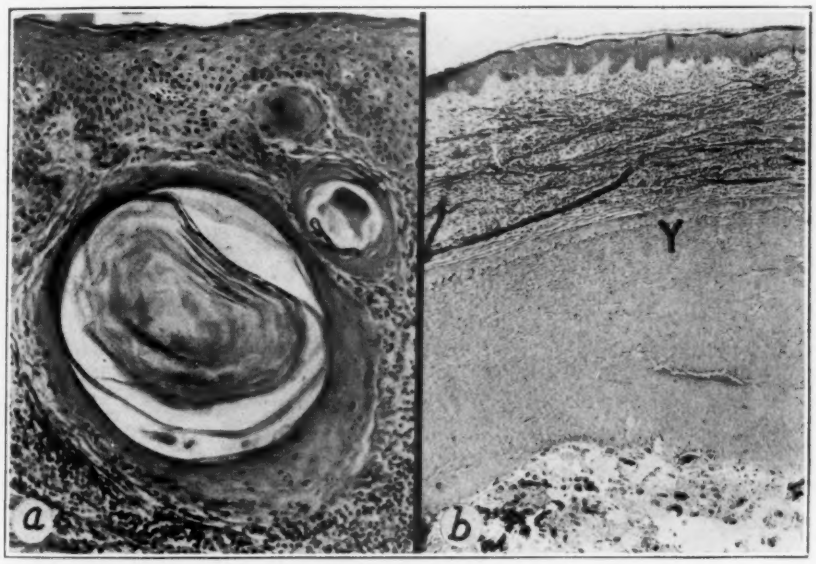

Fig. 4.—Milia (*a*); the structure is similar to that of an epithelial cyst with secondary inflammatory reaction about it (× 100). Sebaceous cyst (*b*); note the vacuolated cells in the wall of the cyst at *y*, lack of keratinization of the wall of the cyst and deposition of calcium in the cyst (× 35).

16. New, G. B., and Erich, J. B.: Dermoid Cysts of the Head and Neck, Surg., Gynec. & Obst. **65**:48-55 (July) 1937.

17. The terms dermoid and epidermoid have been used loosely to include various types of cysts, and certain types of dermoids are equivalent to the term epithelial cysts. We prefer to limit these terms to cysts containing both epidermal and dermal tissue, including epithelium, hair, various of the dermal appendages and even at times the teeth and nails; in other words, dermoid cysts of the teratoma type. The term epidermoid would seem better than dermoid, as the latter would imply inclusion of structures in the true dermis only.

often contain large amounts of cholesterol and crystals and deposits of calcium (fig. 4 *b*). Chemical analysis of the contents of four sebaceous cysts did not show any appreciable increase, however, in the fat content, the mean lipid content being 2.85 per cent, which is within normal limits for the epidermis as a whole. The histologic picture shows the wall of the cyst to be smooth. As a rule, there are no papillary bodies or rete ridges. Definite sebaceous cells can be identified in the wall at varying intervals. The wall is usually only a few layers in thickness. There is no attempt on the part of the basal cells to become keratinized (fig. 4 *b*), and therefore one does not see a laminated keratinized substance. Dubreuilh and Tribondeau [18] found sebaceous cysts capable of secondary budding, and thus they may become multilocular. Siemens [19] and Cockayne [20] have shown that the tissues of certain persons are predisposed to form cysts, the predisposition being inherited as a mendelian dominant characteristic.

Bosellini [21] described steatocystoma multiplex as a rare condition characterized by multiple cystic lesions of varying sizes resulting apparently from plugging of pilosebaceous follicular orifices through hyperkeratosis, which causes retention of sebaceous material in the sebaceous duct. According to Ormsby and Finnerud,[22] the wall of a cyst may be continuous with the epidermis on one side and connected with a lanugo hair follicle on the other. The cysts contain sebaceous material, the larger ones having clear fluid, like olive oil, and the smaller ones containing white cheesy material.

EPITHELIOMA (CARCINOMA) IN EPITHELIAL AND SEBACEOUS CYSTS

The incidence of epitheliomatous changes in sebaceous cysts has been studied by Caylor,[23] who found it to be 3.4 per cent in 236 cases, by Bishop,[24] who obtained 9.2 per cent in 119 cases, and by Stone and

18. Dubreuilh, W., and Tribondeau, L.: Kystes épidermiques prolifères, Ann. de dermat. et syph. **1**:417-432, 1910.

19. Siemens, H. W.: Studien über Vererbung von Hautkrankheiten. V. Atherom—zugleich ein Beitrag zur Klinik der Epidermoide und der Follikularcysten, Arch. f. Dermat. u. Syph. **144**:175-193, 1923.

20. Cockayne, E. A.: Inherited Abnormalities of the Skin and Its Appendages, London, Oxford University Press, 1933, p. 352.

21. Bosellini, P. L.: Beitrag zur Lehre von den multiplen, folliculären Hautcysten, Arch. f. Dermat. u. Syph. **45**:81-95, 1898.

22. Ormsby, O. S., and Finnerud, C. W.: Steatocystoma Multiplex, Arch. Dermat. & Syph. **22**:822-832 (Nov.) 1930.

23. Caylor, H. D.: Epitheliomas in Sebaceous Cysts, Ann. Surg. **82**:164-176 (July) 1925.

24. Bishop, E. L.: Epidermoid Carcinoma in Sebaceous Cysts, Ann. Surg. **93**:109-112 (Jan.) 1931.

Abbey,[25] who obtained an incidence of 2.2 per cent in 363 cases. Distinction between sebaceous and epithelial cysts apparently was not made in any of these series. Caylor's studies were made before Broders and Wilson made the distinction of keratoma (epithelial cyst). We had the opportunity of reviewing 9 of Caylor's original 12 cases of epithelioma arising from sebaceous cysts. In 2 instances the type of cyst was indeterminate because of extensive epitheliomatous changes that had taken place already. Caylor depended on the history given by the patient for the diagnosis of sebaceous cyst in these instances. In 6 of his cases there was squamous cell epithelioma grade 1 to 3 (Broder's method) definitely arising in relation to epithelial cysts. In 1 case a basal cell epithelioma arose from the walls of a sebaceous cyst. Malignant change usually was preceded by ulceration.

Caylor, Bishop and Stone and Abbey all agreed that trauma or irritation either was absent or played a minor role in the development of the epitheliomatous changes. In Bishop's series there were 2 basal cell and 9 squamous cell epitheliomas. One patient was a Negress. In the series of Stone and Abbey, in 4 cases the tumor was of the basal cell type, in 3 of the prickle cell type and in 1 of a mixed type. These authors stated that no epithelioma of the basal cell type occurred in the scalp. Havens[26] has reported the rare instance of a melanoepithelioma in a keratoma (epithelial cyst) which was removed from the forehead. Collins[27] reported 3 cases of carcinoma arising in sebaceous cysts, 1 of which, if one judges from his illustration and clinical history, could better be regarded as a traumatic epithelial cyst of five months' duration on the palmar aspect of the finger.

In our series of 271 cases, there were 4 epitheliomas, or an incidence of only 1.5 per cent. Two of these were basal cell epitheliomas arising from the walls of sebaceous cysts of the forehead in men aged 47 and 57 years, and 2 were squamous cell epitheliomas grade 1 arising from the walls of epithelial cysts (fig. 5), 1 in the sacral region of a woman aged 55 and the other in the scalp of a man aged 61. One would expect that epitheliomas developing in epithelial cysts would be of squamous cell type. They usually run a relatively benign course, but in 1 of Caylor's cases the neoplasm was a wild invasive grade 4 squamous cell

25. Stone, M. J., and Abbey, E. A.: Sebaceous Cyst: Its Importance as a Precancerous Lesion, Arch. Dermat. & Syph. **31**:512-515 (April) 1935.

26. Havens, F. Z.: Removal of Calculi from the Submaxillary Ducts: A Trick in Tying a Knot; a Simplified Method of Local Anesthesia for Removal of Keratomas and Sebaceous Cysts, S. Clin. North America **15**:1227-1232 (Oct.) 1935.

27. Collins, D. C.: Carcinoma Originating in Sebaceous Cysts, Canad. M. A. J. **35**:370-372 (Oct.) 1936.

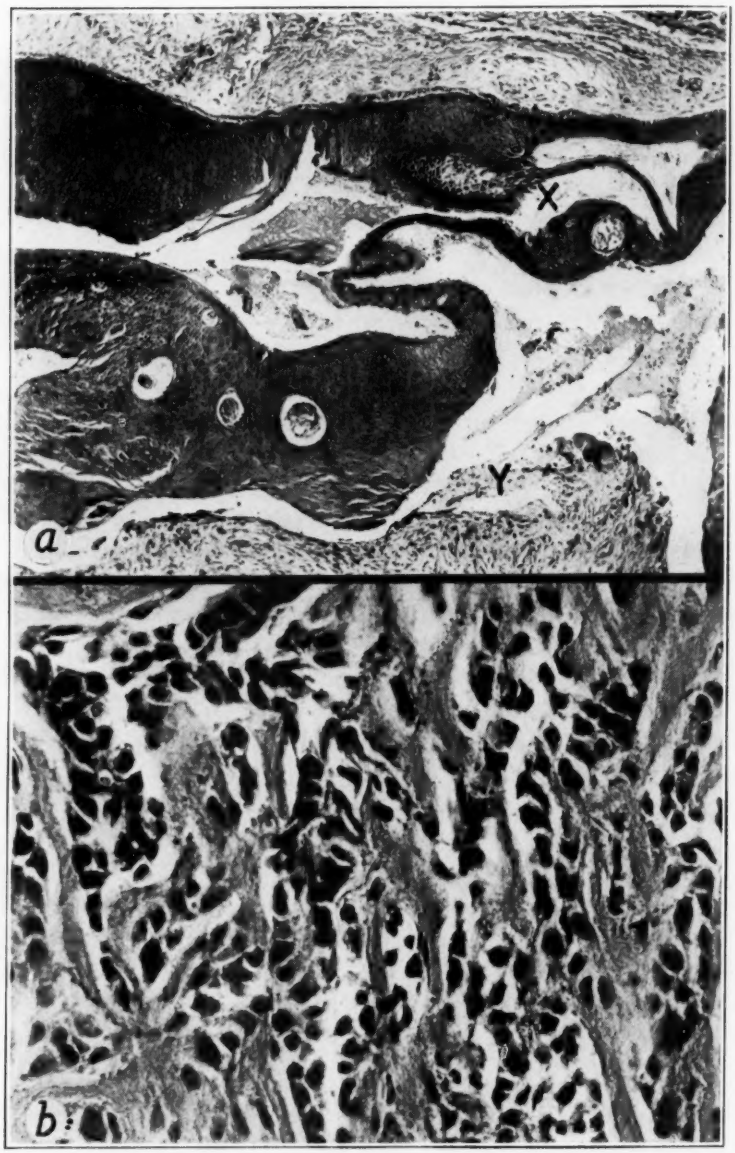

Fig. 5.—Epithelial cyst (*a*) with squamous cell epithelioma grade 1 arising from the wall at *x; y* indicates the interior of the cyst (× 65). Squamous cell epithelioma grade 4 (*b*) situated in the keratinous contents of an epithelial cyst (× 320).

epithelioma which eventuated in metastasis and death of the patient seven months after excision. It seems probable that in most cases that have been reported basal cell epitheliomas arise from sebaceous and not from epithelial cysts. Again, this is to be expected when one considers that basal cells differentiate into sebaceous cells and do not show a tendency toward formation of normal stratified squamous epithelium.[28] It should be stated that generalized steatomas (sebaceous cysts) as described by Cady [29] have not been reported as manifesting malignant change.

One of us (H. M.) [30] has emphasized previously that sebaceous cysts, and that would not include epithelial cysts, are not to be regarded as precancerous lesions, the percentage incidence being no greater than one would expect when one considers the age incidence and various possible precipitating causative factors.

TREATMENT

The treatment of epithelial cysts varies according to their location and size, whether they are infected and whether they have ruptured with resultant fibrosis and adherence to the surrounding structures. The technic of enucleation or excision of these cysts is given in detail by Erich.[31] Sometimes after infection a cyst undergoes complete resolution spontaneously as the result of the destruction of the epithelial lining. As a rule, a cyst should not be excised when showing signs of inflammation but may be incised to hurry the subsidence of the inflammation. Any cyst which shows signs of growth, especially without inflammation, or any cyst showing ulceration should be regarded as potentially malignant and excised widely.

SUMMARY

Epithelial cysts should be distinguished from sebaceous cysts, with which in the past they have been confused. They usually can be distinguished on a clinical basis. Histologic studies, however, are diagnostic and need often be employed. The question of the origin of epithelial cysts as retention cysts in relation to the sebaceous ducts versus

28. Macleod, J. M. H., and Muende, I.: Practical Handbook of the Pathology of the Skin: An Introduction to the Histology, Pathology, Bacteriology and Mycology of the Skin with Special Reference to Technique, ed. 2, New York, Paul B. Hoeber, Inc., 1940, pp. 241-248.

29. Cady, L. D.: A Case of Generalized Steatoma, Arch. Dermat. & Syph. **9**:96-101 (Jan.) 1924.

30. Montgomery, H.: Precancerous Dermatosis and Epithelioma in Situ, Arch. Dermat. & Syph. **39**:387-408 (March) 1939.

31. Erich, J. B.: Sebaceous, Mucous, Dermoid and Epidermoid Cysts, Am. J. Surg. **50**:672-677 (Dec.) 1940.

origin from embryonic epithelial rests is discussed. Epithelial cysts are to be distinguished from milia, sebaceous cysts and steatocystoma multiplex. Neither epithelial cysts nor sebaceous cysts are to be regarded as precancerous dermatoses. If cancer eventuates, it usually is in the form of squamous cell epithelioma when arising from an epithelial cyst and basal cell epithelioma when arising from a sebaceous cyst. As one would expect, epitheliomatous changes in epithelial and sebaceous cysts occur most frequently in the later decades of life. Wide excision is indicated when malignant change is suspected.

SYMMETRIC NEVI OF FACE, TUBEROUS SCLEROSIS, EPILEPSY AND FIBROMATOUS GROWTH ON SCALP

WITH ABNORMAL ELECTROENCEPHALOGRAMS OF MEMBERS OF THE FAMILY; REPORT OF A CASE

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AND
JOHN GARB, M.D.
NEW YORK

We are reporting a case of multiple symmetric nevi of the face with tuberous sclerosis associated with epilepsy and a large fibromatous growth on the scalp. Beside other important features, the abnormal electroencephalographic findings for 4 other members of the family are also presented.

REPORT OF CASE

L. T.,[1] an American-born woman aged 20, of an Italian mother and a French father, not consanguineous, was referred by the North Hudson Hospital, Weehawken, N. J., for treatment at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on June 20, 1940. She presented a large disfiguring growth on the scalp and a prominent red eruption on the face (figs. 1 and 2). She gave a history of frequent epileptic attacks. A "red birth mark" was noticed on the scalp at birth. It was hairless, smooth and level with the surrounding cutaneous surfaces. When she was 9 years of age this birth mark began to grow spontaneously. It grew wider and thicker with age.

Family History.—The maternal grandfather died of an accident; the maternal grandmother was living and well. The paternal grandfather died of "heart failure," and the paternal grandmother died of "cancer of the stomach." One sister died of bronchopneumonia at the age of 11 months. The mother appeared well and healthy. When the patient was born the father was 22 and the mother 23 years old. The mother gave a history of a fall down a flight of stairs while pregnant. "She had a fright when an older child burned her hand with a flat iron." The delivery was spontaneous and at full term.

The patient was the second oldest of 6 girls and the only one to be so affected. One sister, aged 21, was "very nervous and irritable but otherwise normal."

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, clinic of Dr. Fred Wise.

1. The patient was presented before the New York Dermatological Society, Nov. 26, 1940 (Wise, F.: Adenoma Sebaceum [Hallopeau-Leredde Type] with Tuberous Sclerosis, Arch. Dermat. & Syph. **44**:92 [July] 1941) and before the Academy of Medicine, April 1, 1941 (Good, C. K.: Adenoma Sebaceum [Hallopeau-Leredde Type] with Tuberous Sclerosis, ibid. **44**:1125 [Dec.] 1941).

Another, 15 years old, had a congenital deformity of the cervical region of the spine associated with unilateral deafness. Roentgenograms revealed congenital malformation of the cervical portion of the spine with a faulty epiphysial development and a rudimentary left first rib, rotary curvature of the upper dorsal part of the spine and elevation of the left scapula. The deafness began eight

Fig. 1.—Large fibromatous growth on the scalp and small fibromas on the face.

years before, following an infection and discharge from the ear. One sister, aged 12 years, had been having pain in the left hypochondriac and kidney regions. An intravenous urogram revealed bilateral nephroptosis with angulation of the left ureter. She had a slight lateral curvature of the lumbar vertebrae to the left. Examination of the other sisters and parents did not reveal anything of note. The results of serologic tests taken of all of them were negative. The electroencephalographic reports are given in another part of this paper. Frequent

attempts to have the father checked up for the "kidney trouble" were unsuccessful. The patient herself, however, was most cooperative and anxious to undergo all the various tests and examinations.

History of Infancy, Childhood and Adolescence.—The patient weighed 8½ pounds (3,856 Gm.) at birth. She began to sit up at 6 months of age, to walk at 10½ months and to talk at 18 months. She spoke fairly clearly at 2½ years of age. She began to menstruate at 13. The periods were regular, every twenty-eight days, seven days in duration. She had no dysmenorrhea.

Fig. 2.—Front view showing the fibromatous growth ending by sharp line at the outer half of the left eyebrow and the butterfly distribution of the nevoid growths on the face and chin, with relative circumoral pallor.

She did fairly well in school but was poor in English and arithmetic. She was employed in a curtain factory for four years previous to admission to the hospital.

History as Related to Epiloia.—The lesions on the face began when she was 8 months old, soon after an attack of measles. Three tiny pale red pinhead-sized "blotches" appeared first in the left malar region. Some lesions then developed on the root of the nose and on the right cheek and later spread downward on both cheeks as low as the inferior borders of the mandibles and the chin. They

attained their maximum development both numerically and in surface area when she was 3 years of age. At 10 years these "blotches" began to grow, being transformed gradually into "wart-like" projections. After she was 16 years of age the lesions on the mandibles regressed while the remaining fibromatous nodules became larger.

At 4 years of age the patient began to display signs of abnormal nervous irritability. These were supraorbital headaches, biting of the nails, frequent crying spells lasting fifteen to twenty minutes and oft repeated unreasonable and unaccountable acts of stubbornness, followed in a few minutes by a complete change of mood and a ready willingness to cooperate.

The most distressing affliction was the occurrence of convulsive seizures, which came on as often as three to six times a day for two and one-half years. These were typical epileptic attacks occurring irregularly during the day and night and characterized by sudden falling down on the floor and loss of consciousness, with tonic and clonic spasms of the muscles of the trunk and extremities, cyanosis, rolling of the eyes and frothing of the mouth. Sometimes these attacks would be followed by involuntary discharge of urine and feces. After the seizures the patient, exhausted, would usually fall asleep. On awakening she would be as well as before the onset of the convulsion, "as if nothing had happened." When she was 6½ years old these attacks followed in rapid succession, "without a letup," the patient then sinking into a stuporous and unconscious state for two weeks. This cloudy state, or status epilepticus, was a pronounced turning point in her illness. There was general mental improvement. After that she never lost consciousness, but until three or four months before the time of writing she had "nervous spells," when she became frightened and would then "grab anything in front of her." These spells lasted a few minutes. Her memory was better, but the outbursts of stubbornness were still as frequent, lasting about fifteen to twenty minutes if "she did not have her way." For the last six months she blinked her eyes continuously.

Dermatologic Examination.—On the scalp and moving freely with it was a large sharply demarcated almost hairless hard growth, varying in color from grayish white to red. It was oblong and 7½ inches (19 cm.) in length, with the wider and larger "head piece" resting in front of and to the right of the lambda, the growth crossing obliquely to the left of the midline of the scalp and the narrower "tail end" ending by a straight edge at the left supraorbital ridge. With its rounded surface, the many depressions, clefts and convolution-like elevations and the grayish white color, it resembled a calf's brain. It was 5 cm. wide at the frontal region, narrowing to 2.5 cm. at the middle and widening to 9 cm. at the upper end. It varied in depth from 0.2 cm. at the "tail end" to 1 cm. at the middle of the "head part." Projecting from the surface, mostly from the middle third, were numerous small yellowish white rounded cystic nodules. The growth was unevenly divided by horizontal, linear, superficial and deep clefts.

On the middle two thirds of the face, but predominantly on the tip of the nose and in the nasolabial grooves, symmetrically distributed in a butterfly fashion, were pinhead-sized to split pea–sized yellowish brown and purplish red superficial flattened and only slightly raised soft growths. The lesions were aggregated but discrete except in the nasolabial sulci, where they were semiconfluent, forming irregular patches. They felt velvety to the touch and were easily compressible, revealing yellowish stains on diascopic pressure. Intermingled with these growths were numerous raised soft linear pedunculated pinhead-sized to hemp seed–sized fibromas. On the forehead were numerous small yellowish brown pigmented spots which did not fade on pressure. The fibromas were also present on the upper

lip but to a lesser extent, producing a relatively circumoral pallor. The skin of the trunk and extremities, in sharp contrast to the lesions on the face and scalp, was normal in appearance and texture and completely devoid of any nevoid growths. There were no subungual fibromas. Recently the patient called attention to the presence of many filiform verrucous projections on the anterior border of the right axilla.

General Medical and Special Examinations.—The patient was of average height and weight, rather alert, answering many questions about her lengthy history fairly intelligently. She was easily irritated and disturbed. She had frequent episodes of absences with grimacing movements of the face during the

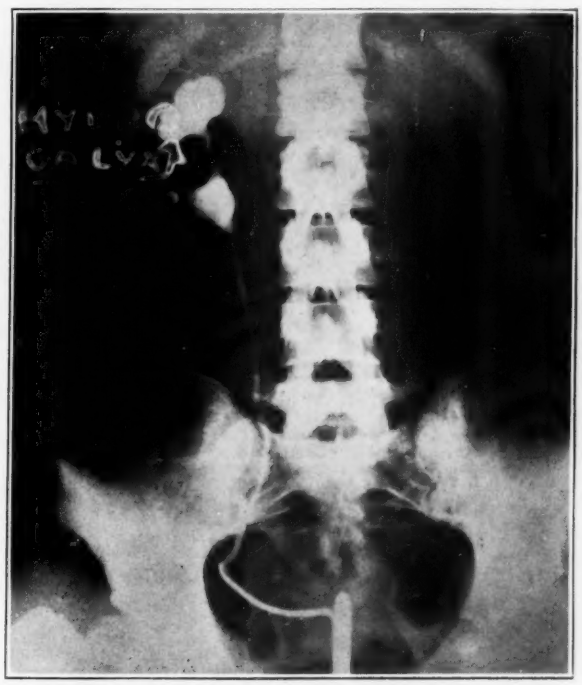

Fig. 3.—Hydrocalix of the right kidney.

time she had her history taken. She did not display bizarre movements of the fingers. She seemed to be in fair physical health. The secondary sex characteristics were well developed. The pupils were 2 mm. in width and reacted well to light and in accommodation. The fundi were normal. There were no tumors or pigmentations of the retina. The deep reflexes were hyperactive, and the right plantar reflex was absent. The results of other routine physical examinations were normal. An electrocardiogram disclosed a fast sinoauricular rate and a slight tendency toward deviation of the axis to the left. The routine laboratory examinations, the lipid partition of the blood serum, determined by the method of Bloor, and the fibrinogen were normal.

Urologic Examination (Dr. Herbert R. Kenyon).—A bilateral retrograde pyelogram (fig. 3) revealed "a narrowing and elongation of the upper calix of

the right kidney with dilatation and blunting of the minor calices. A minute calcified fleck corresponded to the upper pole of the right kidney, requiring verification. The left ureter was deflected medially with a slight angulation below the left ureteropelvic juncture."

On Nov. 14, 1940 the patient was readmitted to the hospital for pain in the right groin and frequency of urination. She vomited once. She had a decided tenderness in the region of the right kidney. A cystogram and a pyelogram again showed normal mucosa and capacity of the bladder and hydrocalix of the right kidney.

Examination of the Brain, Intelligence and Personality.—Roentgenographic examination of the skull by Dr. William H. Meyer did not reveal gross abnormality of the bones of the vault or of the base. The sella turcica was large and smooth, measuring 20 per cent above average size. Examination of the entire spine showed no evidence of osseous or articular abnormality.

A ventriculogram made after injections of air showed that the ventricles were of comparatively normal size and contour. The structural changes in the outer portion of the vault were mainly ascribable to tumefaction of the overlying soft tissue.

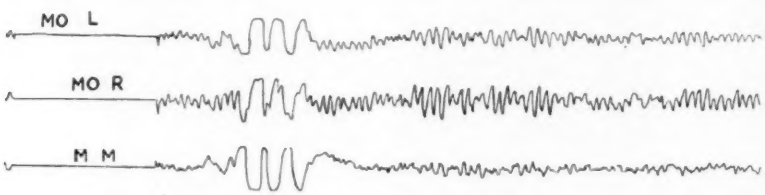

Fig. 4.—Second electroencephalogram of the patient, taken March 26, 1942, which is suggestive of a convulsive disorder.

Electroencephalograms were made of the patient and of all the members of the immediate family by Dr. Bernard L. Pacella. The patient's first electroencephalogram was made on Oct. 9, 1941. It gave a borderline normal record, which pattern "is often seen in convulsive disorders during a quiescent interval."

A record of the second electroencephalogram, taken on March 26, 1942 (fig. 4), "remained essentially the same as noted in the previous examination, with the exceptions that there was a slightly greater incidence of 5 to 7 cycle per second waves bilaterally, and on one occasion a short burst of high amplitude 3 cycle per second potentials appeared synchronously from both sides of the head. A mild degree of diffuse abnormal electrocortical activity was present over the entire cortex. No evidence of a localized lesion was noted. The pattern was suggestive of a convulsive disorder."

Test Behavior: She was fairly cooperative; her responses were slow; her reasoning was poor, and there was poor associative elaboration.

Test Interpretation: The patient obtained a rating of borderline intelligence. Her mental age was 11-3 and her intelligence quotient 75 (with 15 as adult level). Reasoning, memory and numerical manipulations were poor. Planfulness was very low; she lacked alertness. Vocabulary was at a low dull normal level. Associative learning was average with attention difficulties.

Emotional Insight Test: She had a sympathetic attitude, with a tendency toward stubbornness and insistence on having her way, moodiness, concern over health and ready anger.

Histologic Examination.—A small growth was removed from the face and examined histologically. It was diagnosed as fibroma by Dr. Satenstein. The description given by Dr. Charles F. Sims was as follows: "There were many hair follicles, some of which extended downward to the middle and deep parts of the cutis. The cutis consisted of considerable denser collagen bundles in the upper central portion of the section than in the remainder. This density was greatest in the perifollicular zones. These areas contained many spindle-shaped connective tissue cells. The vessels throughout the cutis were moderately dilated. Scattered clusters of brownish pigment were noted in the upper part of the cutis."

A second nodule was later removed from the face, and the following observations were made: "The epidermis presented numerous hair follicles, some of which possessed the so-called *Mantelhaare* of F. Pinkus.[2] The corium showed slight

Rating of Borderline Intelligence (Dr. A. D. Tendler, Nov. 15, 1942): Detailed Report of Special Functions

Function	Year Level
Memory	10
Comprehension of situation	13
Reasoning	9
Verbal ability, vocabulary	12
Numeral manipulation	9
Learning ability	15

Tests Employed		Score	
Test	Capacities Tested	Mental Age	Intelligence Quotient
Terman-Binet	Ideational intelligence	11-3	75
Porteus maze	Planfulness	8	53

increase of the sebaceous glands and fibrous tissue but otherwise no noteworthy changes." Van Gieson's stain failed to reveal anything of note.

Treatment.—On Sept. 20, 1940 the involved area of the forehead and the anterior half of the tumor on the scalp were excised by Dr. Straatsma. The defect was repaired by a full thickness skin graft taken from the left side of the abdomen. The other half of the growth was excised six weeks later. Gross examination of the tumor of the scalp made by Dr. Rabson disclosed numerous nodular areas up to 1 cm. in diameter. On section the cut surface was homogeneously gray and consisted apparently exclusively of light gray dermal tissues. There were several cystic areas up to 0.6 cm. in diameter filled with cheesy material.

Dr. Sims interpreted the histologic structure as fibromatous (fig. 6). He made the following observations: "The epidermis was irregular with numerous short and narrow rete pegs. It was covered in some areas by very slight horny layers, whereas in others no horny layer was visible. There were numerous hair follicles extending downward to the middle and deep parts of the cutis. These follicles were surrounded by a dense collagenous mantle. With high magnification one noted numerous spindle-shaped cells. The blood vessels appeared thickened and dilated. The intimal nuclei projected into the lumen, and in some instances they presented a

2. Pinkus, F., cited orally by H. Bieberstein.

sparse perivascular infiltration composed of plasma cells and occasional small round and wandering connective tissue cells. The sebaceous glands presented no unusual changes."

Examination of the section with Van Gieson's stain failed to reveal neural fibers.

The lesions on the face were gradually destroyed at weekly intervals by electrodesiccation. Local anesthesia with infiltrations of procaine hydrochloride was used.

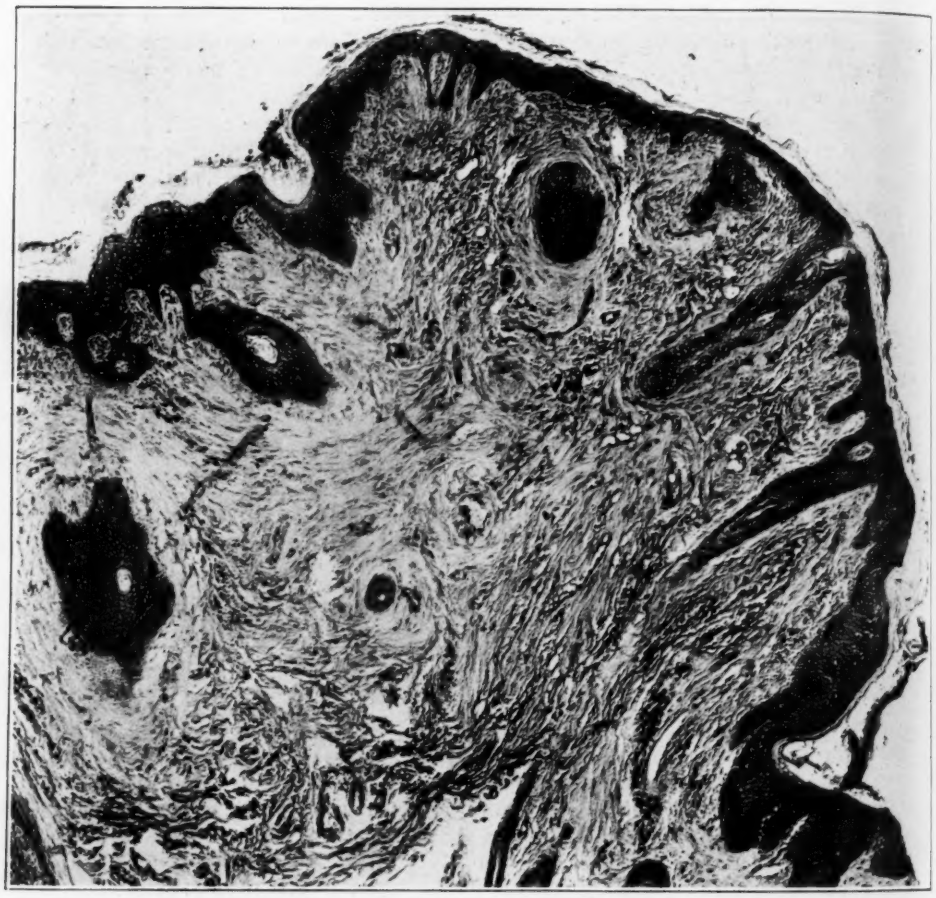

Fig. 5.—Photomicrograph of a fibromatous nodule on the face showing many hair follicles and dense collagen bundles most evident in the perifollicular zones (× 70).

After May 1, 1941 the lesions of the face were treated every two weeks with carbon dioxide slush.

Results.—The scalp now presents a reddish smooth hairless patch extending from the left supraorbital region to the lambda. It has not shown any evidence of recurrence up to the time of writing. The patient covers up this defect with her hair so that only a smooth small, whitish scarred area on the left side of the head is visible.

The lesions on the face consist now of pinpoint-sized to pinhead-sized closely set spots which make her face appear flushed (fig. 7). The results of the treatment can be considered satisfactory.

Fig. 6.—Photomicrograph of the fibromatous growth on the scalp showing numerous hair follicles extending downward to the middle and deep portions of the cutis and surrounded by a dense collagenous mantle (× 20).

Mentally the patient seems improved. Her memory is better. She is, according to her parents, more intelligent, more cheerful and more willing to be with friends.

ELECTROENCEPHALOGRAPHIC EXAMINATIONS OF PARENTS AND SISTERS

Electroencephalograms were made by Dr. Pacella of the parents and the other 5 sisters. That of the father and those of 3 girls showed abnormal findings. The reports are given herein:

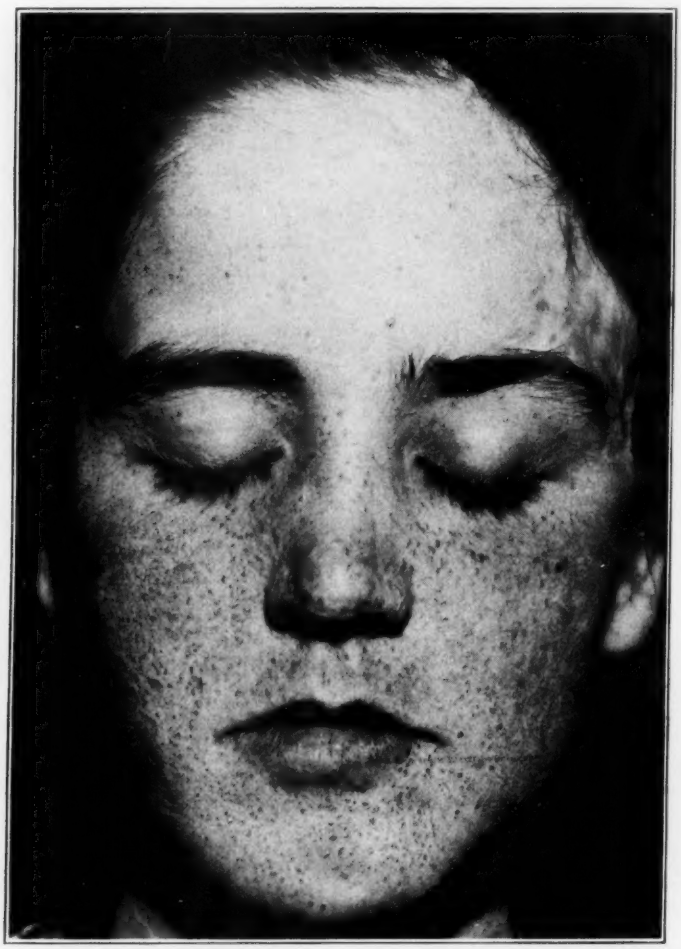

Fig. 7.—Front view of the patient after removal of the growth from the scalp by plastic surgery, destruction of most of the lesions on the face with electrodesiccation and subsequent treatment with carbon dioxide slush.

The electroencephalogram of W. T., the father, aged 42 (fig. 8 *A*), showed low amplitude, irregular activity with beta rhythm over the anterior regions, while a high amplitude, high incidence 9 cycle per second rhythm was noted over the parietal and occipital areas. Hyperventilation resulted in the occasional appearance of 5 to 6 cycle per second potentials, with one or two short runs of 5.5 cycle per

second waves of high amplitude bilaterally over the parieto-occipital areas. There were no significant bilateral differences. There was a mild degree of diffuse abnormal electrocortical activity over the parieto-occipital areas bilaterally. The character of the pattern was not suggestive of any focal abnormality but might very well be consistent with a "latent" convulsive disorder. Similar patterns are frequently encountered in blood relatives of persons with epilepsy.

The electroencephalogram of T. T., a sister aged 22 (fig. 8 *B*), showed irregular activity in the frontal areas with moderate amplitude 8 to 10 cycle per second waves appearing at random and much beta rhythm. The parietal and occipital regions

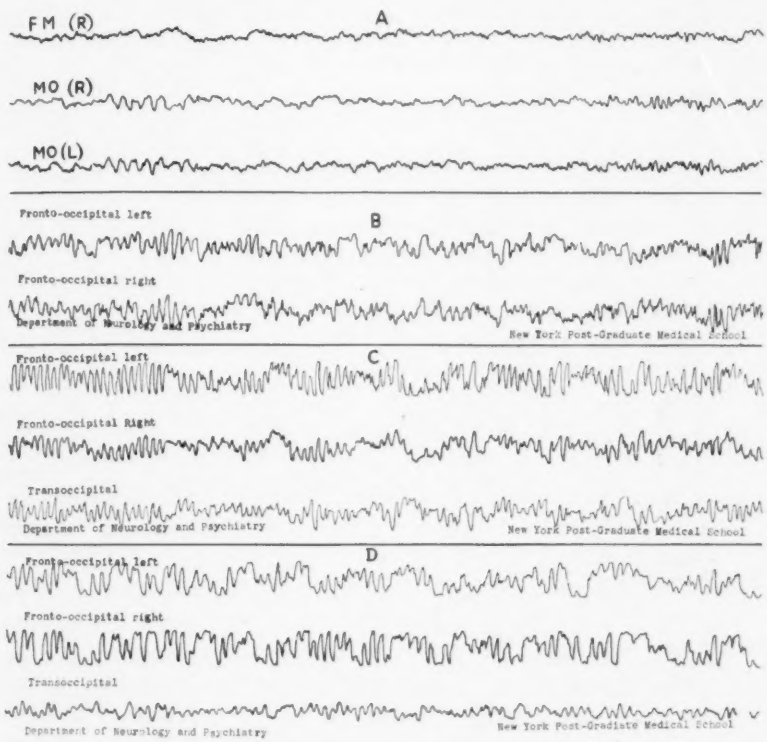

Fig. 8.—Reproductions of electroencephalograms of (*A*) W. T., the father, which may be consistent with a latent convulsive disorder; (*B*) T. T., a sister, the pattern of which is highly consistent with a clinical diagnosis of a convulsive disorder; (*C*) E. T., a sister, the pattern of which is highly consistent with a clinical diagnosis of a convulsive disorder, and (*D*) J. T., a sister, which reveals the presence of a mild degree of diffuse abnormal electrocortical activity.

showed a high incidence of high amplitude 9 to 11 cycle per second waves with occasional short "trains" of 7 to 8 cycle per second potentials. Hyperventilation resulted in frequent appearance of 5 to 6 cycle per second potentials of increased amplitude over all regions of the cortex and random occasional 3 to 4 cycle per second waves bilaterally. There were no significant bilateral differences. An impression of diffuse abnormal electrocortical activity was given. The character of the pattern was consistent with a clinical diagnosis of a convulsive disorder.

The electroencephalogram of E. T., a sister aged 18 (fig. 8 *C*), showed irregular low to moderate amplitude activity in the frontal areas with a mixture of some beta rhythm and short trains of irregularly shaped 8 to 10 cycle per second waves. Frequent 5 to 8 cycle per second waves were noted at random bilaterally. The parietal and occipital regions exhibited predominantly high amplitude 10 to 11 cycle per second waves and frequent 5 to 7 cycle per second potentials bilaterally. Hyperventilation produced an increase in the incidence of 5 to 7 cycle per second waves all over regions of the cortex, with the frequent random appearance of 3 to 4 cycle per second waves of high amplitude, particularly over the frontal areas.

There was diffuse abnormal electrocortical activity of only moderate severity, appearing relatively more pronounced over the anterior regions bilaterally. The character of the pattern was highly consistent with a clinical diagnosis of a convulsive disorder.

The electroencephalogram of J. T., a sister aged 16 (fig. 8 *D*), showed a 9 to 9.5 cycle per second alpha rhythm of moderate to high amplitude which predominated over the parietal and occipital regions bilaterally, with the random appearance of 4 to 6 cycle per second waves of high amplitude synchronously from both sides of the head. The frontal regions exhibited irregular activity, with a mixture of beta rhythm and moderate amplitude 9 to 10 cycle per second potentials. Hyperventilation increased very definitely the incidence of the 4 to 6 cycle per second waves and also resulted in some irregularity of pattern. The slow potentials appeared most frequently over the anterior regions of the cortex. A mild degree of diffuse abnormal electrocortical activity was present. No suggestion of a focal lesion was noted.

COMMENT

Historical Review and Morbid Anatomy.—Von Recklinghausen [3] in 1863 was probably the first to recognize the pathologic changes in tuberous sclerosis. He found sclerotic areas in the brain and several myomas in the heart muscle of a newborn child. Bourneville [4] in 1880 demonstrated sclerotic growths in the cerebral cortex of a 3 year old girl with retarded growth, "acne rosacea" of the face, epilepsy and idiocy. He was the first to describe this syndrome and named it "tuberose," or "tuberous," sclerosis because of the potato-like resemblance of these growths in shape, appearance and consistency. This syndrome is sometimes referred to as "Bourneville's tuberose sclerosis." Numerous authors have since contributed largely to this subject.

These tumors occur scattered on the surfaces of the frontal lobes. They may be found in other parts of the brain and occasionally in the cerebellum, medulla, spinal cord [5] and retina, those in the last-mentioned

3. von Recklinghausen, F.: Ein Herz von einem Neugeborenen welches mehrere theils nach aussen, theils nach den Höhlen prominierende Tumoren (Myomen) trug, Verhandl. d. Gesellsch. f. Geburtsh. **15**:73, 1863; cited by Butterworth and Wilson.[15]

4. Bourneville: Scléreuse tubéreuse des circonvolutions cérébrales: Idiotic et épillepsie hémiplégique, Arch. de neurol. **1**:81, 1880-1881.

5. Critchley, M., and Earl, C. J. C.: Tuberose Sclerosis and Allied Conditions, Brain **55**:331 (Sept.) 1932.

place being described by van der Hoeve [6] as phakomas. They occasionally project downward into the third and lateral ventricles, arising usually from the thalamus and resembling grapes or "candle gutterings." [7] They sometimes produce symptoms of cerebral tumors.[8] The growths may vary from one to thirty in number and from 0.5 to 3 cm. in diameter. The smaller tumors are usually located on a summit of a gyrus and limited to the boundaries of a convolution, while the larger growths may extend to two or three convolutions and may then involve the summit of the gyrus as well as the depth of the sulci. Some of the viscera, particularly the heart and kidneys and more rarely the lungs, liver, pancreas, intestines, spleen, bone, bladder and retina, may contain cystic tumors or myomas.[9] Hall [10] reported a case of tuberous sclerosis associated with rheostosis of the hand.

Microscopic examination reveals that the pathologic process in the brain is much more widespread than that seen by the naked eye and that the zones between the foci show pronounced changes which differ only in degree from those of the tubera. Changes are also found in other regions of the central nervous system, especially in the cerebellum and the spinal cord. The main histologic features are the presence of peculiar giant cells and a proliferation of the neuroglia with corresponding atrophy of the nerve element. Some of the giant cells resembled giant nerve cells, while others are thought to be primitive glial elements. Most histologists [11] believe that these cells represent undifferentiated embryonal cells of the spongioblastic and neuronic varieties.

Epiloia and the Members of the Triad Complex.—To the complete triad of mental deficiency, epilepsy and adenoma sebaceum Sherlock [12] applied the term epiloia to stress the epidermal origin of the main structures. But any two or one only of the symptoms of the triad may be present, or retinal or visceral tumors may occur alone as formes frustes, which are common among the members of the family or relatives of a person with epiloia.

When tuberous sclerosis occurs alone there may be no symptoms or physical signs to indicate its presence until the development of ade-

6. van der Hoeve, J.: Augengeschwülste bei der tuberösen Hirnsklerose (Bourneville), Arch. f. Ophth. **105**:880, 1921.

7. Lind, cited by Critchley and Earl,[5] p. 331.

8. Walsh, M. N.; Koch, F. L. P., and Brunsting, H. A.: Syndrome of Tuberous Sclerosis, Retinal Tumors and Adenoma Sebaceum, Proc. Staff Meet., Mayo Clin. **13**:155 (March) 1938.

9. Walsh, Koch and Brunsting,[8] p. 156.

10. Hall, G. S.: Tuberose Sclerosis, Rheostosis, and Neurofibromatosis, Quart. J. Med. **9**:1 (Jan.) 1940.

11. Critchley and Earl,[5] p. 342.

12. Sherlock, E. R., cited by Hopwood.[23]

noma sebaceum in later life, the onset of a convulsion, the occurrence of insanity in middle life or sudden death [13] in a member of the family of a patient with epiloia.

When adenoma sebaceum occurs alone in persons with normal intelligence who have never had epileptic seizures there is still the possibility, according to Critchley and Earl,[14] "that slight nervous or mental changes might be present though not obvious on cursory examination. . . . [and] that slight alterations might be found in the cortex of such individuals, differing only in degree from those occurring in epiloia." These authors stated that they could not find records of the cerebral changes in cases of adenoma sebaceum alone, but the existence of latent cerebral changes is intimated by the occasional development of insanity in middle life in these patients.

Butterworth and Wilson [15] stated the belief that in some cases mental deficiency alone may possibly be due to tuberous sclerosis. Only by encephalographic studies or by the observation of typical "candle gutterings" in the ventricle or on postmortem examination could the diagnosis be made. They have so far been unable to find case reports of feeblemindedness alone which could be explained on the basis of tuberous sclerosis. We have been reviewing the literature and inquired personally of specialists in this field of study and thus far have been unable to get any data on that subject.

Electroencephalography as an Important Contribution to the Hereditary and Familial Study of Tuberous Sclerosis.—The hereditary and familial character of tuberous sclerosis has long been known and confirmed. Epiloia or any one or two of the elements of the triad has frequently occurred in the members of the families of persons with epiloia, or the hereditary influence has been characterized by mild neurologic symptoms, psychic taint, muscular spasms, visceral lesions or cutaneous manifestations, which may vary from adenoma sebaceum to warts, muscular atrophy or fibromas. Without going into discussion about the value of electroencephalograms in other abnormal conditions of the brain, its usefulness in the study of epilepsy has been definitely proved. Gibbs [16] expressed the following opinion:

> About 10 per cent of the supposedly normal population have cerebral dysrhythmias, and these are only slightly or not at all different from the interseizure dysrhythmias of epileptic patients. . . . These cases of asymptomatic dysrhythmias are in fact cases of asymptomatic epilepsy.

13. Critchley and Earl,[5] pp. 316 and 340.

14. Critchley and Earl,[5] p. 340.

15. Butterworth, T., and Wilson, M. Jr.: Dermatologic Aspects of Tuberous Sclerosis, Arch. Dermat. & Syph. **43**:1 (Jan.) 1941.

16. Gibbs, F. A.: Diagnostic and Prognostic Value of the Electroencephalogram, J. A. M. A. **118**:216 (Jan. 17) 1942.

Davis [17] stated:

> Equally important is the fact, now fairly well established, that the cerebral dysrhythmia is a hereditary characteristic that is almost always to be found in the epileptic individual himself and among his blood relatives. Here, apparently, is the hereditary element in epilepsy—the potentiality for seizures that is far more common and widespread in the population than the incidence of actual seizures.

Besides the patient, the father and 3 other sisters revealed abnormal electroencephalographic changes, or 4 out of 7, 57 per cent, of the members of her family. While it is true that abortive forms of tuberous sclerosis could be suspected in the father, because of his frequent indulgence in alcoholic beverages and the history of "kidney trouble," in T. T. (fig. 8 *B*), because she had been "nervous and irritable," and in J. T. (fig. 8 *D*), because of the possible relationship to epiloia of the congenital deformity of the cervical region of the spine and the unilateral deafness, abnormal electroencephalographic findings of a convulsive disorder, perhaps on the basis of tuberous sclerosis, would ordinarily not be looked for in E. T. (fig. 8 *C*), who was apparently normal in every respect. The electroencephalogram may therefore prove to be a valuable diagnostic aid for discovering abortive types of tuberous sclerosis in members of the family and close or distant relatives of a person with epiloia in whom there are no evident mental or neurologic symptoms and signs, cutaneous manifestations or visceral lesions.

It is worth mentioning that the first electroencephalogram of the patient reported on, made on Oct. 9, 1941, showed "a borderline normal record," while the second, on March 26, 1942, was "suggestive of a convulsive disorder." This shows that the electroencephalogram may vary at different periods and that more than one recording is necessary to discover abnormalities. This has been expressed by Strauss, Rahm and Barrera,[18] who stated:

> Since abnormal potentials are not always present and cannot always be produced by hyperventilation, even in overt epileptics, it is possible that abnormal records in some of the examined subjects were missed.

While these electroencephalograms do not show characteristics different from those patterns obtained from persons with idiopathic epilepsy, it is possible that other cases and special study might show distinct features which would differentiate this condition from other types of convulsive disorders, as symptomatic epilepsy has frequently been differentiated from idiopathic epilepsy. Gibbs [16] stated that the localization of a tumor of the brain, localized infection or area of trauma may be deduced from

17. Davis, H.: Electroencephalography, J. A. M. A. **117**:983 (Sept. 20) 1941.

18. Strauss, H.; Rahm, W. E., Jr., and Barrera, S. E.: Electroencephalographic Studies in Relatives of Epileptics, Proc. Soc. Exper. Biol. & Med. **42**:207 (Oct.) 1939.

the part of the cortex that shows maximal disorder. When a lesion is truly cortical such localizations are about 90 per cent accurate.

Etiology.—This case fits in with the usual history of the occurrence of tuberous sclerosis in the "lower classes" of the community. The father was a heavy drinker and of average intelligence. In our case, as well as in 1 of the cases of Critchley and Earl,[19] there was a history of labor preceded by a fright. There was no definite family history of tuberous sclerosis except the death of the paternal grandfather of "heart failure," which may have been due to a rhabdomyoma. The "kidney trouble" of the father may possibly have been a renal tumor. He refused to have a urologic examination. T. T. (fig. 8*B*) revealed a psychic taint by being irritable and nervous. The congenital deformity of the spine and the unilateral deafness of J. T. (fig. 8*D*) may have had some relationship to epiloia.

Scarpatetti [20] regarded parental syphilis as the cause of tuberous sclerosis. All writers on this subject now agree in eliminating syphilis as a factor in this syndrome. The Wassermann reactions of the spinal fluid and blood of the patient were normal. The Wassermann and Kahn reactions of all the members of the immediate family were negative. The subjects were examined and found free of any possible syphilitic infection.

The theory has been proposed [21] that tuberous sclerosis might be an embryologic metabolic disorder of lipid metabolism because of the presence of lipid deposits in the brains of some patients with that disease. It is of interest to note that in our case as well as in a case reported by Walsh [21] the lipid partition of the blood was normal. Normal blood cholesterol, though, could occur with lipid disturbance as a member of the normocholesteremic group of the xanthomatous diseases.[22] Critchley and Earl [11] advanced the views that tuberous sclerosis may be considered as a hyperplastic disorder of the neuroglia originating during embryonic life and associated with hyperplasias in other extramural structures or as a widespread metaplasia which affects mainly the ectodermal tissues and to some extent endodermal and mesodermal derivatives, having its origin in utero.

Clinical Variations of the Patient Reported On.—The lesions are usually reported as appearing first in the nasolabial folds.[23] In our case they commenced in the left malar region as three tiny pale red

19. Critchley and Earl,[5] p. 315.

20. Scarpatetti, cited by Critchley and Earl,[5] p. 315.

21. Walsh, Koch and Brunsting,[8] p. 157.

22. Thannhauser, S. J.: Lipidoses: Diseases of the Cellular Lipid Metabolism, edited by H. A. Christian, New York, Oxford University Press, 1940, p. 43.

23. Hopwood, A. T.: Tuberous Sclerosis: Report of Five Cases Including One Case in One of Twins, Ohio State M. J. **33**:277 (March) 1937.

blotches, from which they spread to the root of the nose and the right cheek and then downward on both cheeks.

Sessile fibromatous growths have been reported in cases of multiple symmetric nevi of the face.[24]

Renal tumors have been reported found in 80 per cent of cases of tuberous sclerosis.[25] They are rarely diagnosed during life. Our patient showed a narrowing and elongation of the upper calix of the right kidney with dilatation and blunting of the minor calices. Is this abnormality related to tuberous sclerosis or only a coincidence?

It is generally stated that the earlier the signs and symptoms appear in a person with epiloia the more rapid is the course. Critchley and Earl [26] stated:

> The course of the epiloiac is rapidly downhill after puberty; death usually takes place in the second decade from cachexia, pulmonary disease or status epilepticus. . . . One striking feature in many epiloiacs—which distinguishes them from other cases of epilepsy with mental defect—is the very long periods of remission which may be present. [These periods of freedom may last for many years and are independent of treatment.] . . . During these remissions the mental deterioration usually continues steadily, thus emphasizing the lack of correspondence between the severity of the epilepsy and of the idiocy.

These authors reported 1 case out of a series of 29 in which the remission lasted seven years and there was no mental impairment.

The patient began to have convulsive attacks at the age of 4 years and lapsed into a state of status epilepticus at 6½ years. After that she had frequent fleeting seizures only. Contrary to the progressive mental deterioration following the letup in the convulsions that usually occur in tuberous sclerosis, our patient showed an improvement in her mental condition and displayed a more cheerful attitude. She became less irritable and more cooperative and mingled more readily with people. This may be attributed to the improvement in her physical appearance caused by the removal of the growth on the scalp and the destruction of the fibromas of the face.

Classifications.—The cutaneous lesions of the face were originally diagnosed as adenoma sebaceum of the Hallopeau-Leredde type.[1] The first slide revealed that the growth was made up mostly of fibrous tissue. There were few sebaceous glands. A second specimen for biopsy taken later showed an increase in sebaceous glands and fibrous tissue of only a little more than in the normal skin of the face. We feel, therefore, that these growths belong more properly to the group

24. Beck, S. C.: Epitheliome: Morbus Pringle (Adenoma Sebaceum Pringle), in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1933, vol. 12, pt. 3, p. 482.

25. Critchley and Earl,[5] p. 339.

26. Critchley and Earl,[5] pp. 316-318.

named *naevi symétriques de la face* by Hallopeau or that named *nevi symmetrici multiplici faciei (multiple symmetrische Gesichtsnaevi)* by Jadassohn.[27]

The term epiloia has been applied by Sherlock [12] to the triad of adenoma sebaceum, mental deficiency and epilepsy to connote the epidermal origin of these structures. Since the growths on the face in our case are fibromas, which are derived from mesodermal tissue, the term epiloia could not strictly be applied.

Prognosis as to Life.—Campbell [28] gave statistics of deaths for 77 patients with tuberous sclerosis. Twenty-two, or 29 per cent, died before the age of 5 years. Between the ages of 16 and 20 there were 11 deaths; between 21 and 25, 9; between 26 and 30, 6, and over 30, 4. Most of the patients with tuberous sclerosis die before the age of 20; few live to over 30. One of Lind's patients [29] lived to the age of 47.

SUMMARY AND CONCLUSIONS

A patient with multiple symmetric nevi of the face with tuberous sclerosis, epilepsy and a large fibromatous growth on the scalp is described. The patient also had a hydrocalix of the right kidney. The father and 3 out of 5 sisters revealed abnormal electroencephalographic tracings consistent with clinical diagnoses of convulsive disorders.

The progress in this case was contrary to the usual progressive mental deterioration noted in patients with this condition with the letup of the epileptic seizures. The patient showed an apparent improvement in her mental state and behavior following status epilepticus. The improvement in her general physical appearance following the removal of the tumor of the scalp and the fibromas of the face no doubt contributed largely to her more pleasant attitude and behavior.

The growth appeared first in the left malar region instead of in the nasolabial groove as usually reported. The patient and the entire family were examined and found negative for any possible syphilitic infection. The lipid partition of the serum was entirely normal. This does not obviate the theory advanced by some investigators that tuberous sclerosis might be an embryonic lipid disturbance of the brain, as a lipid disease could occur with normal lipid partition of the blood as a member of the normocholesterol group of xanthomatous diseases.

The electroencephalogram may be a useful diagnostic aid in discovering formes frustes of tuberous sclerosis in members or relatives of

27. Beck,[24] pp. 478-491.

28. Campbell, cited by Cockayne, E. A.: Inherited Abnormalities of the Skin and Its Appendages, London, Oxford University Press, 1933, pp. 289-293; cited by Butterworth and Wilson.[15]

29. Lind, W. A. T.: Epiloia, M. J. Australia (supp.) **1**:290 (June 14) 1924.

persons with epiloia who show no evidence of mental, neurologic or cutaneous changes.

The opinion is advanced that perhaps by further study of groups of patients with tuberous sclerosis, types of patterns may be obtained which would differentiate this disease from other types of convulsive disorders just as symptomatic epilepsy can frequently be differentiated from idiopathic epilepsy.

The father, who gave a history of "kidney trouble," probably had renal tumors, which may present a forme fruste of tuberous sclerosis. A sister with a spinal deformity and unilateral deafness perhaps had osseous changes referable to the aforementioned syndrome.

The large fibromatous growth was successfully removed by plastic surgery, and the fibromatous nodules of the face were removed by electrodesiccation and then followed by applications of solid carbon dioxide every two weeks. The result was gratifying.

More than one electroencephalogram is sometimes necessary to establish abnormal findings of a convulsive disorder, as the electroencephalogram will vary at different periods and may be normal at certain times even for persons with overt epilepsy.

While the case has been previously presented as one of adenoma sebaceum of the Hallopeau-Leredde type of tuberous sclerosis further sections revealed histologic structures which fit in more properly with naevi symétriques de la face of Hallopeau or naevi symmetrici multiplici faciei of Jadassohn.

Miss Clare Holzer, of the social service department, assisted in performing all the various tests and examinations, and Miss Eleanor Engs, of the photographic department, prepared the photomicrographs and the reproductions of the electroencephalograms.

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STUDIES ON OINTMENTS

III. OINTMENTS CONTAINING SULFUR

ERNEST A. STRAKOSCH, M.D.
MINNEAPOLIS

Unna [1] expressed the opinion that all substances which are capable of withdrawing oxygen from the tissue promote the process of keratinization and are what he termed keratoplastic. Besides the purely chemical action, however, Jadassohn [2] pointed out that other factors, biologic and physical, have to be considered.

Sulfur, because of its keratolytic, keratoplastic, antipruritic and antiparasitic action, is one of the most important drugs in dermatology and a common constituent of many pastes, ointments, lotions and proprietary remedies. The dermatologist is most interested in the local action of sulfur. I attempted to compare the local action of sulfur in various concentrations in different bases. Before going on with the report of my findings, a short review of the pharmacologic action of sulfur, as far as it is known, will be given.

THE PHARMACOLOGIC ACTION OF SULFUR

Elementary sulfur occurs in many modifications, which differ from each other in physical properties, such as melting point, specific gravity and the forms of crystals. These different characteristics depend on the differences in the size of the sulfur molecule: at a low temperature S_8, then S_4, at a temperature above 900 C. S_2, and at 1500 C. beginning of dissociation into atoms, according to Oppenheimer.[3] Sulfur is a yellow, crystalline, hard substance and is insoluble in most solvents. It dissolves

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The third condensed part of a thesis, submitted to the faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Dermatology and Syphilology.

1. Unna, P. G.: Ueberhautung und Ueberhornung, Berl. klin. Wchnschr. **35**:533, 1883.

2. Jadassohn, J., cited by Perutz, A., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1930, vol. 1, p. 143.

3. Oppenheimer, C.: Grundriss der anorganischen Chemie, Leipzig, Georg Thieme, 1927, p. 186.

in hydrogen sulfide at 15 C. to 37 per cent and at 55 C. to 151 per cent, and, according to Moncorps,[4] it dissolves at a 10 per cent concentration in olive oil to 0.58 per cent and in lard to 0.92 per cent.

The three preparations of the Pharmacopeia of the United States, washed, precipitated and sublimed sulfur, differ, according to Heubner,[5] only in their degree of purity and are principally of the same chemical modification or a mixture of identical modifications.

Sulfur occurs in the body in cysteine:

$$\begin{matrix} CH_2 - SH \\ CHNH_2 \\ COOH \end{matrix}$$

Thioaminopropionic acid

which is the carrier for sulfur. By means of condensation and oxidation of it, the cystine is formed:

$$\begin{matrix} CH_2 & -S & -S & -CH_2 \\ CHNH_2 & & & CHNH_2 \\ COOH & & & COOH \end{matrix}$$

di-(thioaminopropionic acid)

It has been known for a long time that cysteine may be readily oxidized to cystine. The carrier of the "thiol group," —R.SH, in the tissue besides cysteine is the glutathione of Hopkins,[6] which is a tripeptide, containing cystine, glutamic acid and aminoacetic acid.

In the air, and especially in the presence of light, the elementary sulfur is oxidized first to sulfurous acid and later to sulfuric acid. The lowest phase of oxidation is hydrogen sulfide (H_2S).

De Rey-Pailhaide [7] reported in 1888 that if animal tissue is brought into contact with sulfur, hydrogen sulfide is formed. This observation was later closely studied by Heffter [8] and by Hausmann and Heffter,[9]

4. Moncorps, C.: Untersuchungen über die Pharmakologie und Pharmakodynamik der Salben und salbeninkorporierten Medikamente, Arch. f. exper. Path. u. Pharmakol. **141**:50 and 87, 1929.

5. Heubner, W.: Chemie und Pharmakologie des Schwefels, Zentralbl. f. Haut- u. Geschlechtskr. **20**:385, 1926.

6. Hopkins, F. G.: (*a*) On an Autoxidisable Constituent of the Cell, Biochem. J. **15**:286, 1921; (*b*) Glutathione: Its Influence in the Oxidation of Fats and Proteins, ibid. **19**:787, 1925.

7. De Rey-Pailhaide, cited by Heffter, A., and Heubner, W.: Handbuch der experimentellen Pharmakologie, Berlin, Julius Springer, 1927, vol. 3, p. 1.

8. Heffter, A.: Beitrag zur Pharmakologie des Schwefels, Arch. f. exper. Path. u. Pharmakol. **51**:175, 1904.

9. Hausmann, M., and Heffter, A.: Ueber die Wirkung des Schwefels auf Eiweisskörper, Beitr. z. chem. Physiol. u. Path. **5**:213, 1904.

who found it to be the cysteine which forms hydrogen sulfide if brought into contact with sulfur. Glutathione acts likewise.

The biochemistry of sulfur and the pharmacodynamic of that substance are extremely complicated, and Heubner,[5] Heffter,[8] Hausmann and Heffter,[9] Hopkins,[6] Sabbatini [10] and Wieland [11] made investigations which demonstrated clearly that the action of sulfur depends on its conversion to hydrogen sulfide, which has a keratolytic effect. If sulfur comes in contact with living tissue, then hydrogen sulfide is formed.

Pulewka [12] pointed out that the degree of swelling and keratolysis of the epidermis depended partly on the hydrogen ion concentration. He found a decided increased swelling and keratolysis of the stratum corneum from sulfhydrate when the p_H was above 10.8, while its action below that p_H was much less. Gans [13] was able to show that the p_H in the uncornified epidermis changes considerably. He found average p_H values in cases of oozing eczema to be 7.5, while in cases of psoriasis and dry eczema the p_H was 6.8. He then pointed out that the alkaline reaction of the tissue was the reason why the application of sulfur in an acute inflammatory process causes aggravation, for sulfur shows its optimal effect in an alkaline medium, causing swelling of the cells and inflammation. In psoriasis, on the other hand, the acid tissue reaction diminishes the action of sulfur.

The keratoplastic effect is the second feature of the sulfur action. Unna assumed a reducing effect of sulfur, which he thought responsible for the keratoplastic action. But it is an oxidation process in reality, for Heubner [5] showed the important fact that the elementary sulfur behaves principally like oxygen, acting on the thiol group and transforming cysteine into cystine, the latter forming the most important constituent of the keratin substance. As sulfur is capable of bringing about this transformation, it promotes the formation of keratin and therefore acts as a keratoplastic.

The absorption of sulfur as well as its reexcretion through the skin in the form of hydrogen sulfide has been studied by Moncorps,[4] Maliwa,[14]

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10. Sabbatini, L.: Ueber die Wirkung des kolloidalen Schwefels je nach dem Weg der Einführung in den Organismus, Biochem. Ztschr. **59**:378, 1914.

11. Wieland, H.: Ueber den Mechanismus der Oxydationsvorgänge, Ergebn. d. Physiol. **20**:477, 1922.

12. Pulewka, P.: (*a*) Die hornlösende Wirkung der Schwefilalkalien, Ztschr. f. physiol. Chem. **146**:130, 1925; (*b*) Weitere Untersuchungen über Keratolyse, Arch. f. exper. Path. u. Pharmakol. **140**:181, 1929.

13. Gans, O.: Ueber die Bedeutung des Schwefels für die Biologie und Pathologie der menschlichen Haut, Zentralbl. f. Haut- u. Geschlechtskr. **20**:388, 1926.

14. Maliwa E.: Beiträge zur experimentellen Balneologie der Schwefelbäder, Med. Klin. **22**:851 and 1764, 1926.

Bier [15] and many other investigators. Moncorps investigated the absorption of sulfur from various ointment bases and found the least absorption from zinc paste; absorption then increased in succession with an oil in water emulsion, a water in oil emulsion and petrolatum to the best lard. Bechhold [16] and Milbradt [17] pointed out that the absorption of sulfur depends on the degree of dispersion in the ointment base. The work of Brandrup,[18] who showed that sulfur is in a molecular solution in lard and olive oil and only partly so in paraffin and petrolatum and least of all in hydrous wool fat, is therefore of interest. von Hahn [19] demonstrated that colloidal sulfur has only a local action and penetrates little if at all.

The absorption of sulfur from various bases has some practical interest, especially in the treatment of children, for an increased absorption may be accompanied by constitutional symptoms and has even led to death, as reported by Burmeister [20] and Basch.[21]

EXPERIMENTAL STUDIES

Precipitated sulfur was incorporated in the strength of 1, 3, 5, 10, 15 and 20 per cent into the following bases: (1) petrolatum; (2) petrolatum and hydrous wool fat in equal parts; (3) a base consisting of 6 per cent of a group of esters of cholesterol chiefly oxycholesterol in an aliphatic hydrocarbon petrolatum base [22]; (4) a base consisting of fatty acid esters of diethanolamine mixed with petrolatum,[23] and two bases whose

15. Bier, A.: Der Schwefel, München. med. Wchnschr. **72**:1621, 1930.

16. Bechhold, H.; Ornstein, S., and Silbereisen, K.: Zur Reaktionsfähigkeit von Schwefel verschiedener Dispersität, Dermat. Wchnschr. **89**:1539, 1929.

17. Milbradt, W.: Zur Frage der Anwendung echter Schwefellösungen in der Therapie der Hautkrankheiten (Sulfupront), München. med. Wchnschr. **84**: 1492, 1937.

18. Brandrup, W.: Ultramikoskopische Untersuchungen über das System: Salbengrundlage salbeninkorporierter Schwefel, Apoth. Ztg. **48**:993, 1933.

19. von Hahn, F. V.: Kolloidalwissenschaft und Dermatologie, Zentralbl. f. Haut- u. Geschlechtskr. **21**:385, 1926-1927.

20. Burmeister, J.: Ein Fall von Schwefelwasserstoffvergiftung bei einem Krätzekranken nach Anwendung von Pottasche-Schwefelsalbe, Arch. f. Dermat. u. Syph. **58**:389, 1901.

21. Basch, F.: (*a*) Schwefelwasserstoffvergiftung nach Behandlung der Säuglingskabies mit Schwefelsalben, Monatschr. f. Kinderh. **32**:239, 1926; (*b*) Ueber Schwefelwasserstoffvergiftung bei äusserlicher Applikation von elementaren Schwefel in Salberform, Arch. f. exper. Path. u. Pharmakol. **111**:126, 1926.

22. The preparation used was aquaphor, manufactured by the Duke Laboratories Inc., Stamford, Conn.

23. The preparation was hydrosorb, manufactured by the Abbott Laboratories, North Chicago, Ill.

formulas are as follows: (5) stearyl alcohol [23a] 10.0 Gm., liquid petrolatum 10.0 cc., water 10.0 cc. and light petrolatum 70.0 Gm.; (6) zinc oxide 7.5 Gm., talc 7.5 Gm. and enough petrolatum to make 30.0 Gm. The technic used was that previously described.[24]

The histologic changes in the skin after the application of sulfur have been studied by Kopytowsky,[25] who used 10, 25 and 50 per cent sulfur in petrolatum and applied it to the skin of the scrotum for two to four days.

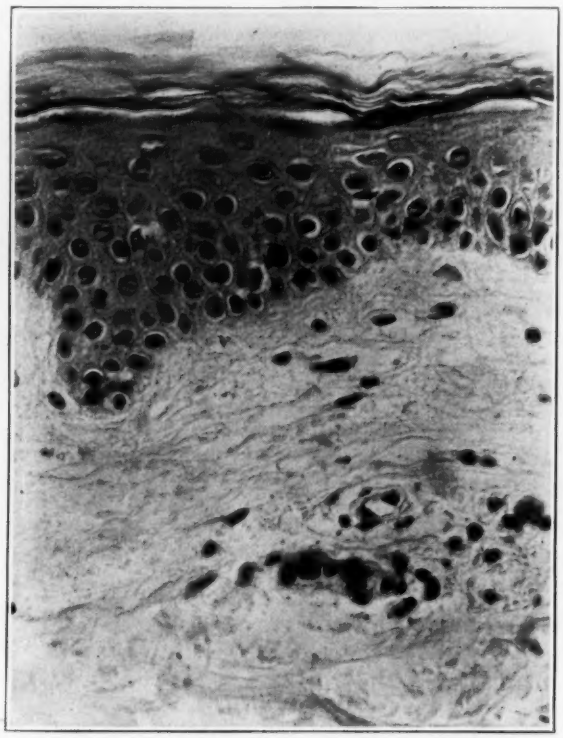

Fig. 1.—Section showing the effect of 1 per cent sulfur in petrolatum and hydrous wool fat (equal parts) after seven days. Note the slight swelling of the stratum corneum.

The changes observed are briefly summarized as follows: There is a swelling of the stratum corneum, which leads to a separation of the

23a. The preparation used was lanette wax, SX, supplied by R. F. Revson Company, New York.

24. Strakosch, E. A.: Studies on Ointments: II. Ointments Containing Salicylic Acid, Arch. Dermat. & Syph. **47**:16 (Jan.) 1943.

25. Kopytowsky, W.: Beitrag zur den pathologischen Veränderungen der gesunden Haut nach Schwefelwirkung, Arch. f. Dermat. u. Syph.. **114**:89, 1912.

lamellas and finally to keratolysis. The granules of keratohyalin in the cells of the stratum granulosum are sometimes absent and often irregularly distributed or accumulated to form small lumps. The chromatic structure in the nucleus of the cells of the stratum granulosum are often absent, or the chromatin arrangement is irregular. There is a decided intercellular and intracellular edema in the stratum spinosum. The stratum basale is thickened, and there is a tendency to acanthosis. The stratum papillare is edematous, the vessels are dilated and the endothelium

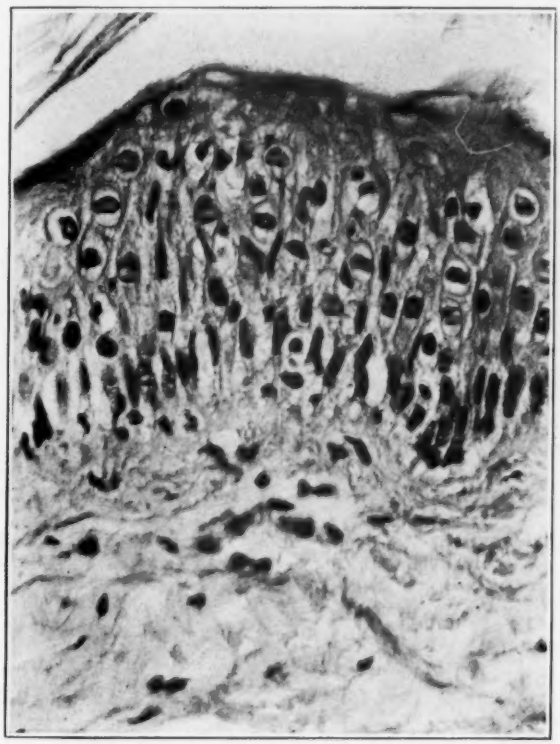

Fig. 2.—Section showing the effect of 5 per cent sulfur in an oxycholesterol-petrolatum ointment base after ten days. Note the keratolysis and the intracellular and intercellular edema.

cells are hypertrophic. The capillaries are dilated and filled with erythrocytes and sometimes with leukocytes; lymphocytes, plasma cells and eosinophils can be found in the dilated tissue spaces.

The changes are indicative of an inflammatory process with proliferative changes in the blood vessels. Hand in hand with it goes an increased formation of keratin substances. The process of keratinization is atypical and incomplete, as indicated by the parakeratosis and the

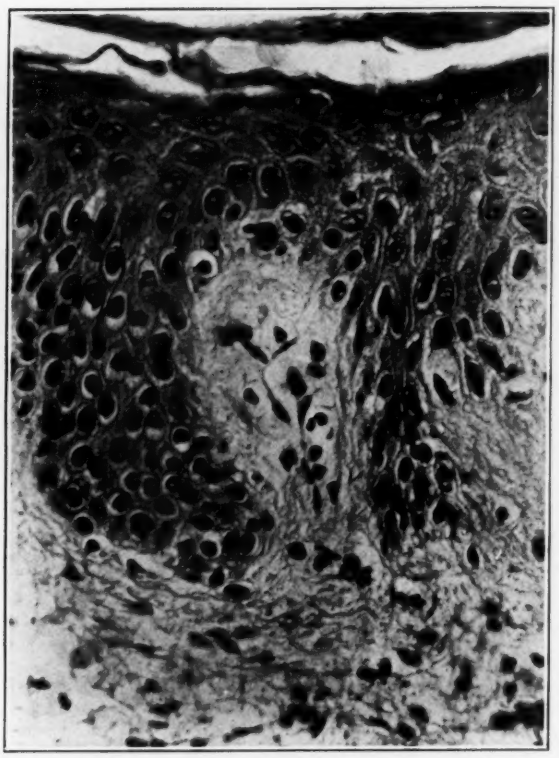

Fig. 3.—Section showing the effect of 10 per cent sulfur in an oxycholesterol-petrolatum ointment base after three days. Note the beginning of the keratolysis, keratoplastic changes, intracellular and intercellular edema, signs of acanthosis and papillary edema.

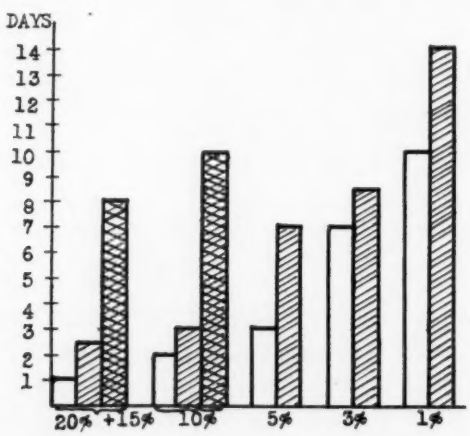

Fig. 4.—Beginning of keratolytic changes. The blank bars indicate petrolatum; the bars with diagonal lines, the oxycholesterol-petrolatum ointment base, the base consisting of fatty acid esters of diethanolamine in petrolatum, the petrolatum and hydrous wool fat base and the base containing stearyl alcohol in liquid petrolatum, water and petrolatum; the bars with diagonal crisscross lines, zinc paste.

keratohyaline changes in the stratum granulosum (keratoplastic changes); keratolytic and keratoplastic changes run parallel, but the latter are more outspoken.

These findings were always present. The intensity of the process and the time necessary to produce them varied depending on the sulfur concentration and the ointment base in which it was applied. An attempt to tabulate the beginning of the keratolytic and keratoplastic changes has been made in figures 4 and 5. The results shown in these tables represent the average findings of four experiments. Each series of experiments was made on the same person, and each series was repeated four times on different persons. The experiments made with 20 per cent sulfur in the same bases showed results similar to those with 10 and 15 per cent concentrations, but the results were somewhat stronger.

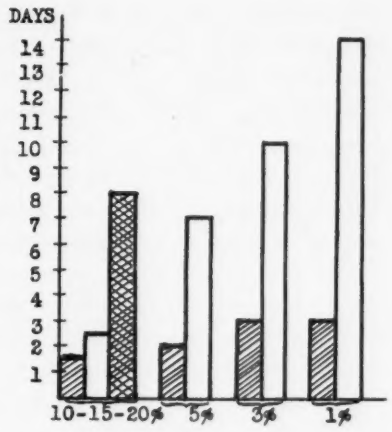

Fig. 5.—Beginning of keratoplastic changes. The blank bars indicate petrolatum; the bars with diagonal lines, the oxycholesterol-petrolatum ointment base, the base consisting of fatty acid esters of diethanolamine in petrolatum, the petrolatum and hydrous wool fat base and the base containing stearyl alcohol in liquid petrolatum, water and petrolatum; the bars with diagonal crisscross lines, zinc paste.

COMMENT

The action of sulfur is mainly twofold, keratoplastic and keratolytic. These two processes run somewhat parallel. Unna believed that a keratolysis occurred only when the stratum corneum was thin or in cases of idiosyncrasy to sulfur, a theory to which I cannot subscribe. It is true that there are persons who have an idiosyncrasy to the drug, and the reactions encountered in those will be more severe than usual, but the keratolytic effect of sulfur can be observed in any one.

Kopytowsky, who spoke almost only of the keratoplastic action of sulfur, had only 8 cases and used the skin of the scrotum for his

experiments. His findings cannot be generalized, as the scrotal skin differs in many forms from the skin elsewhere on the body.

It can be noted in figures 4 and 5 that the best keratolytic action from sulfur was obtained when it was incorporated in petrolatum. This is in sharp contrast to the findings with salicylic acid.[24] The keratoplastic action was better and occurred sooner in lower concentration when sulfur was incorporated in emulsion bases. The type of emulsion appears to be irrelevant. The relation between concentration and time necessary to produce the changes are identical with those discussed in a previous publication [24] and need no further comment.

The interpretation of these findings is difficult, especially in the light of Moncorps's work; he reported a much better absorption of sulfur from petrolatum than from the emulsion bases. It is generally assumed (!) that the keratolytic effect is due to a superficial action of sulfur on the stratum corneum. Hydrogen sulfide is formed, which causes keratolysis, while the keratoplastic changes are due to a deeper action of sulfur on the stratum germinativum. In the latter case, the sulfur would first have to be absorbed and act from the stratum papillare. This assumption gets some support from the fact that keratoplastic changes can be produced by giving sulfur orally, in which cases it goes via the blood stream to the skin, or by giving it subcutaneously, but keratolytic changes by these methods of application have not been reported.

Whether the greater keratolytic and the lesser keratoplastic effect of sulfur in petrolatum compared with the effects of the drug in the emulsion bases can be explained in the light of the poorer penetration of petrolatum is hard to say. It would be a logical explanation. Petrolatum penetrates the skin much more slowly [26] and therefore affords a better surface action for the incorporated drug; ergo the better keratolytic effect on the surface. The emulsion bases penetrate much faster and with them the incorporated drug (?); therefore the better keratoplastic action. This explanation, however, would entirely disregard Moncorps's findings of the better absorption of sulfur from petrolatum. All my histochemical experiments along this line were unsuccessful. There are as yet too many unknown factors to allow any good explanation. Further histochemical and microchemical investigations must first be made to throw more light on this interesting question.

SUMMARY

1. The pharmacologic action of sulfur on the skin has been discussed.

2. Precipitated sulfur was incorporated in strengths of 1, 3, 5, 10, 15 and 20 per cent in the following bases: (1) petrolatum; (2) petrolatum and hydrous wool fat in equal parts; (3) an oxycholesterol-petrolatum

26. Strakosch, E. A.: Studies on Ointments: I. Penetration of Various Ointment Bases, to be published.

ointment base; (4) fatty acid esters of diethanolamine in petrolatum; (5) stearyl alcohol in liquid petrolatum, water and petrolatum, and (6) zinc oxide in talc and petrolatum. Biopsies were performed after one, two, three, seven, ten and fourteen days, and the keratolytic and keratoplastic action of these ointments on normal human skin was studied histologically.

3. The relation of the different concentrations of sulfur in the aforementioned bases to the onset of the keratolytic and keratoplastic changes was studied. The best keratolytic effect was found, under the experimental conditions described, when sulfur was incorporated in petrolatum. The keratoplastic action was better and occurred sooner in lower concentration when sulfur was incorporated in emulsion bases. The type of emulsion appeared to be irrelevant.

3409 Emerson Avenue South.

TREATMENT OF SYPHILIS WITH PHENARSINE HYDROCHLORIDE

PRELIMINARY REPORT

WILLIAM E. LONG, M.D.*
BOSTON

The therapeutic efficiency of any arsenical preparation for the treatment of syphilis is judged largely from the response of early syphilis (primary and secondary) to its use. In order to evaluate a new drug the most important factors to consider are: (1) the rapid control of infectiousness, (2) the healing of lesions, (3) the rate and permanence of serologic response, (4) the prevention of infectious or serologic relapse and progression of the disease, (5) low incidence of involvement of the central nervous system in early syphilis, (6) a beneficial effect on late syphilis and (7) a low incidence of untoward or toxic reactions. A drug which would meet these requirements would indeed be ideal.

Arsphenamine is, even today, the most active of the arsenical preparations in common use, and yet, because of the difficulties encountered in its administration and its untoward effects, it has been largely replaced by drugs which are easier to give and at the same time are less toxic, even though some therapeutic efficiency may have been sacrificed. A new era in the therapy of syphilis was opened by Tatum and Cooper [1] and by Foerster and his associates [2] with the revival, in the form of mapharsen, of arsenoxide, a preparation which Ehrlich and Hata [3] had discarded because they believed it to be too toxic. However, since its introduction it has been widely accepted and has been awarded high

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*Squibb Fellow in Medicine.

This study was made possible by a grant from the E. R. Squibb and Sons Company, New Brunswick, N. J.

From the Evans Memorial, Massachusetts Memorial Hospitals, and the Department of Medicine, Boston University School of Medicine.

1. Tatum, A. L., and Cooper, G. A.: An Experimental Study of Mapharsen (Meta-Amino Para-Hydroxy Phenyl Arsine Oxide) as an Antisyphilitic Agent, J. Pharmacol. & Exper. Therap. **50**:198 (Feb.) 1934.

2. Foerster, O. H.; McIntosh, R. L.; Weider, L. M.; Foerster, L. M., and Cooper, G. A.: Mapharsen in the Treatment of syphilis, Arch. Dermat. & Syph. **32**:868 (Dec.) 1935.

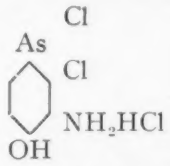
3. Ehrlich, P., and Hata, S.: Die experimentelle Chemotherapie der Spirillosen, Berlin, Julius Springer, 1910.

acclaim.[4] Another drug, phenarsine hydrochloride, which is similar in its structure and belongs to the arsenoxide series of drugs, has been prepared. This new preparation has been studied experimentally in animals and subjected to clinical trial by Tompsett, Downs, McDermott and Webster,[5] who have reported on its toxic effects and clinical behavior. This report presents the results of the use of phenarsine hydrochloride in the treatment of 96 patients with syphilis in the Massachusetts Memorial Hospital clinics.

Phenarsine hydrochloride is a mechanical mixture of 1 part by weight of 3-amino-4-hydroxyphenyldichloroarsine hydrochloride and 3⅓ parts of dry sodium citrate added as a buffer. It is readily soluble in water, physiologic solution of sodium chloride and dextrose solutions, giving a clear, colorless solution which deepens to a faint yellow on standing.

The arsenical portion of this mixture contains 25.8 per cent of arsenic, while the final mixture contains 5.96 per cent. When dissolved in water the p_H of the solution is approximately 5.2.

The structural formula of phenarsine hydrochloride is represented as follows:



When phenarsine hydrochloride is dissolved in water the chlorine atoms are hydrolyzed so that when it is injected it becomes essentially arsenoxide, or its hydrated form, which is generally considered to be the active breakdown product of the arsphenamines in the body. By the addition of sodium citrate the acid arsenical portion is well buffered, and there is a reduction in the toxicity.[1]

Phenarsine hydrochloride is given by intravenous injection after being dissolved in sterile distilled water or saline or dextrose solution.

CLINICAL STUDY

The material of this report represents the data on 96 patients with syphilis who have received treatment with phenarsine hydrochloride for varying periods of time during the past twenty months. The distribution of the cases and the number of injections by groups are summarized in table 1. During the period covered by this report, 2,033 injections of phenarsine hydrochloride were administered.

4. Stokes, J. H.; Beerman, H., and Ingrem, N. R., Jr.: The Trivalent Arsenicals in Syphilis, Am. J. M. Sc. **201**:611 (April) 1941.

5. Tompsett, R. R.; Downs, W. G.; McDermott, W., and Webster, B.: The Use of Clorarsen in the Treatment of Syphilis, J. Pharmacol. & Exper. Therap. **73**:412 (Dec.) 1941.

Phenarsine hydrochloride was given in courses of twelve weekly injections, each course being alternated with one of ten to twelve weekly injections of bismuth subsalicylate in oil. The initial dose for both men and women was 45 mg.; subsequent doses were 67 mg. In a few instances a reduction of dosage was indicated because of the persistence of mild but annoying reactions. When the dose was lowered to 30 mg. injections were given twice weekly. In cases of early syphilis (in which there were infectious lesions) more intensive treatment was given. These patients received 67 mg. every third day for the first two weeks.

In order to determine the spirocheticidal activity, dark field preparations of surface lesions were examined at twelve hour intervals following

TABLE 1.—*Distribution of Cases*

Diagnosis	Number of Cases		Number of Treatments	
	Active	Lost	Active	Lost
Early syphilis (28 cases)				
Seropositive primary syphilis	3	0	103	0
Secondary syphilis	17	4	447	28
Early latent syphilis	8	2	202	11
Late syphilis (39 cases)				
Late latent syphilis	23	14	591	118
Asymptomatic neurosyphilis	7	2	183	49
Active neurosyphilis	3	..	86	..
Active cardiovascular and neurosyphilis	2	..	60	..
Asymptomatic neurosyphilis and chorioretinitis	1	..	24	..
Gumma of skin of nose and septum	1	1	22	7
Late congenital (asymtomatic)	2	2	48	23
Gumma of skin of leg	..	1	..	4
Gumma of pharynx	..	1	..	12
Periostitis	..	1	..	4
Glossitis	..	1	..	11
Totals	67	29	1,766	267
	96		2,033	

the initial injection of phenarsine hydrochloride. After the disappearance of Spirochaeta pallida from the surface lesions, the rate of healing was observed.

In order to observe the serologic response of these patients, each serum was tested quantitatively by the Kline flocculation technic. In addition, Wassermann (Kolmer modification), Kahn and Hinton tests were made on each specimen for confirmation.

In addition to these laboratory observations, a careful study was made in order to determine whether or not toxic reactions followed the use of this drug.

RESULTS OF TREATMENT

Seropositive Primary Syphilis.—During the period covered by this report 3 cases of seropositive primary syphilis were observed. Each patient was given an initial dose of 45 mg. of phenarsine hydrochloride, and this was followed by dark field examination at twelve hour inter-

vals. S. pallida was not found in any of these 3 cases during an examination twelve hours after the first injection. The primary lesions were healed by the tenth day in each instance. The serologic reactions all became entirely negative in three months or less (chart 1). There has been no sign of either progression or relapse of the disease over a period of eighteen months. The spinal fluids are normal.

Secondary Syphilis.—Sixteen cases of secondary syphilis are included in this report. In 7 of these dark field examination of material from the lesions gave positive results on the patient's admission to the hospital. There was a reexamination in 3 twelve hours after the initial injection of phenarsine hydrochloride and in 4 twenty-four hours after-

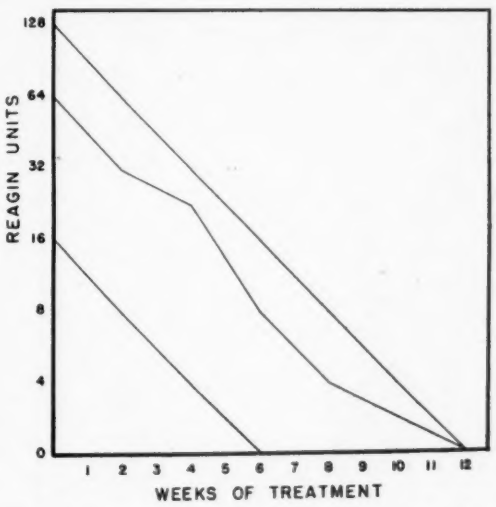


Fig. 1.—Serologic response noted in 3 cases of seropositive syphilis (quantitative Kline test).

ward. No spirochetes were observed at the time of the second examination.

Resolution and healing of the lesions present were rapid. Complete healing was delayed beyond ten days in 1 case in which extensive condylomata lata and secondary infection were present.

The trend in the response of the serologic examinations made on this group of patients is represented in chart 2. In 9 the serologic reaction became completely negative by the sixth month or before. In 3 it became negative between the sixth and the eighth month. Of the 4 remaining cases, in 2 the serologic reaction was doubtful and in 2 it remained positive. In the 2 in which the reactions were doubtful there had been reversal of the Wassermann, Kahn and Hinton reactions but the Kline test still gave a doubtful reaction in undiluted serum. All

four tests continued to give positive results in the other 2 cases. One patient whose serologic reaction remained positive had a positive reaction of the spinal fluid (group I), which accounted for the fact that the reagin titer had shown only a moderate decrease and had remained at a somewhat high level. The spinal fluids of the other 15 patients were normal.

The circumstances of another patient with secondary syphilis who was seen too recently to be included with the group reported on justify special comment. This patient gave a history of a primary lesion on his penis three months before being seen in this clinic. He was treated

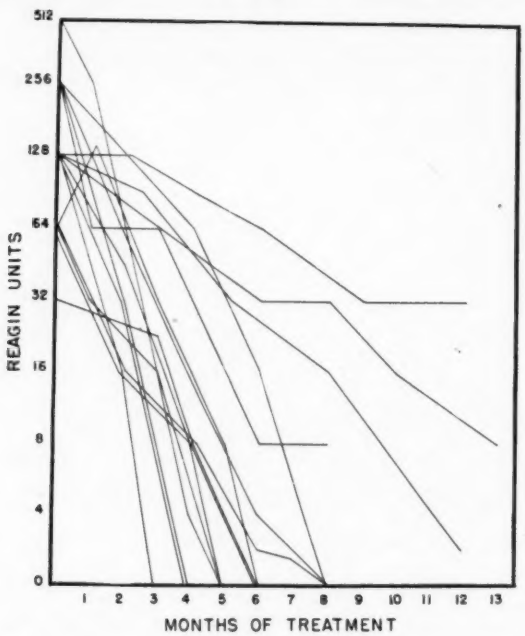


Fig. 2.—Serologic response noted in 16 cases of secondary syphilis (quantitative Kline test).

at home with ointments and did not seek medical attention until the appearance of a generalized eruption, which began seven weeks after the onset of his initial lesion. During a five week period he received nine injections of two of the arsenicals in common use and three intramuscular injections of a bismuth compound, without any effect on the eruption. When the patient was first seen there were large annular lesions on the face, circinate lesions on the forearms and rupial lesions on the back and thighs. The Wassermann, Kahn, Kline and Hinton reactions were all positive. An initial dose of 67 mg. of phenarsine hydrochloride was given. The lesions underwent prompt resolution

and were healed after the fifth injection, in two weeks' time. Subsequent observation has revealed no evidence of continued progression or relapse of the disease.

Early Latent Syphilis.—Three of this group of 8 patients have had a serologic reversal within twelve months (chart 3). In 1 the serologic reaction has been reduced to doubtful, and in 4 it has remained positive. Three of the 4 patients with remaining positive reactions have been irregular in their visits for treatment. A fourth had an initial moderate decline in reagin titer, and after surgical intervention (lobectomy) for a bronchiectatic abscess the titer ran to its former level; it has since made no decline. The spinal fluids of this group are all normal.

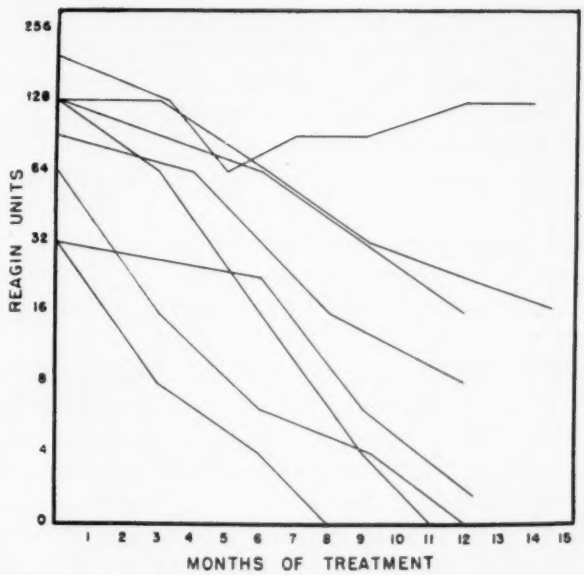


Fig. 3.—Serologic response noted in 8 cases of early latent syphilis (quantitative Kline test).

Late Latent Syphilis.—Twenty-three patients with latent syphilis have been treated for periods varying from four to twenty months. Only 4 of these have had a reversal of the serologic reaction: 2 in six to twelve months and 2 in twelve to eighteen months. Eight others have had a significant decrease in reagin titer, while the serologic reactions of 11 have remained unchanged. In this group an average of 25.7 injections have been given each patient. Many patients have been irregular in attendance for treatment. In general, the degree of serologic response in this group has been proportional to the amount of drug received and the length of treatment. The spinal fluids of these 23 patients are normal.

In all the patients of this group there were decided improvement in general health and a gain of 8 to 12 pounds (3.6 to 5.4 Kg.) of weight in each during the first course of treatment with phenarsine hydrochloride.

Late Symptomatic Syphilis.—In table 1 various late manifestations of syphilis are recorded. There are 16 patients included in this group: 7 with asymptomatic neurosyphilis, 3 with active neurosyphilis with spinal fluids in groups 1 and 2 as outlined by Moore,[6] 1 with asymptomatic neurosyphilis and chorioretinitis, 2 with active cardiovascular syphilis and neurosyphilis (aortitis in 1 and aortic insufficiency in the other), 1 with active gumma of the nasal septum (not perforated) and the skin over the bridge of the nose and 2 with late congenital syphilis without activity.

The 7 patients with asymptomatic neurosyphilis have as a group had no decrease of reagin content of their serum, and the spinal fluids have not been reexamined because the patients have not continued treatment long enough for us to expect any change. They have all remained symptom free, have gained weight and have continued at their employment.

The patient with asymptomatic neurosyphilis and chorioretinitis has had reduction of her serologic reaction from positive to doubtful; however, there has been a progressive diminution of vision in the one affected eye.

The 2 patients with aortic lesions have had remarkable symptomatic improvement and have tolerated full doses of phenarsine hydrochloride without reaction. There has been decided symptomatic improvement in the changes of the central nervous system without alteration in the spinal fluid.

The patient with gumma of the nasal septum and skin of the nose has had complete healing. The reagin content of the serum has greatly decreased. The spinal fluid is normal.

The 2 patients with congenital syphilis have had no serologic response. The spinal fluid of each is normal.

Cases Lost from Observation.—Twenty-nine cases have been lost from observation, and an analysis of their records is of little value; however, some remarks about them should be added. They are classified in table 1.

In the early stages S. pallida was seen to disappear as rapidly as noted in the other cases in which there were early superficial lesions. Healing of all lesions occurred rapidly and completely. Some of the patients had decided reduction of serologic titer before being lost from

6. Moore, J. E.: The Modern Treatment of Syphilis, Springfield, Ill., Charles C Thomas, Publisher, 1941, chap. 31, p. 346.

observation, while some of the others received only a few treatments, and no change was noted. None of these have returned with clinical relapse.

The late lesions, present in some, showed prompt and complete healing.

TOXIC EFFECTS

The reactions to treatment with phenarsine hydrochloride have been mild, and none of the severe type was encountered. Fifty-one patients had no reactions and no complaints from the treatment. Forty-five patients had one or more reactions, making a total of 336. These are recorded in table 2.

As might be expected, gastrointestinal reactions were the most frequent, but in only 3 of the patients were these severe enough to warrant

TABLE 2.—*Reactions from 2,033 Injections of Phenarsine Hydrochloride*

Type of Reaction	Number of Reactions
Gastrointestinal	
Nausea	201
Vomiting	55
Diarrhea	17
Abdominal cramps	7
Headache	4
Pain in arm	8
Depression	2
Malaise	20
Salivation (lasting 5 to 10 minutes, 1 patient)	21
Pruritus	1
Total	336

discontinuance of administration of the drug. These same 3 patients were intolerant to other arsenicals as well. For only a few of the other patients was it necessary to decrease the dosage in order to avoid further reaction. A Herxheimer effect was noted in 7 of the patients with early syphilis and was severe in only 1. Jaundice, cutaneous reactions, blood dyscrasias and nitritoid crises were not seen in any of this series of patients.

COMMENT

The results obtained thus far in the treatment of syphilis with phenarsine hydrochloride indicate that its therapeutic effects are equal to those obtained from any of the arsenicals in general use and that the toxic effects and untoward reactions produced are definitely less frequent and less severe.

In the use of phenarsine hydrochloride for routine treatment certain advantages are offered. With its injection there is no nauseating odor produced, which is characteristic of other arsenicals; for this reason immediate reactions, especially nausea and vomiting, are notably minimal.

Nausea is the most frequent objectionable factor encountered; it is delayed from thirty minutes to an hour and is usually not severe. Since the element of "speed shock" is absent, small amounts of water may be used to dissolve the drug and small caliber needles for its intravenous administration. As little as 2 cc. of water in a hypodermic syringe given with a hypodermic needle has been used to advantage, especially in those patients whose veins are difficult to enter with larger instruments. These factors are minor from the scientific point of view, yet they are important in holding patients to treatment.

SUMMARY

A new trivalent arsenical preparation, 3-amino-4-hydroxyphenyldichloroarsine hydrochloride, known as phenarsine hydrochloride, has been subjected to a clinical test in the treatment of 96 patients with syphilis. A total of 2,033 injections have been gvien over a period of twenty months.

The following observations were made: S. pallida rapidly disappeared from infectious lesions; healing of all lesions, both early and late, was rapid and complete; there was no instance of clinical or infectious relapse; the rapidity of serologic reversal was on the whole satisfactory, and there was a low incidence of abnormal spinal fluids among the patients with early syphilis.

In the group of patients with manifestations of late syphilis, tolerance has been good, symptomatic improvement has been noted and the results have been entirely satisfactory. Toxic reactions have been few, chiefly in the form of mild gastrointestinal disturbance. None of the more severe forms of toxic reaction have been noted.

These results as presented indicate that phenarsine hydrochloride is a potent antisyphilitic drug of low toxicity. Its properties are such as to justify its general use and extended studies carried out in larger groups of patients and over long periods of time.

The serologic studies for this report were carried out in the laboratory of Dr. David L. Belding and Miss Beulah Merrill, of Boston University School of Medicine.

65 East Newton Street.

PHENARSINE HYDROCHLORIDE IN THE TREATMENT OF SYPHILIS

PRELIMINARY REPORT

WILLIAM H. GUY, M.D.

BERNHARD A. GOLDMANN, M.D.

AND

GEORGE P. GANNON, M.D.

PITTSBURGH

For a number of years it has been known that arsenoxide is the effective end product of arsphenamine and neoarsphenamine which produces the curative results in the treatment of syphilis. This drug was produced by Ehrlich in his experiments with various compounds of arsenic but was never used as such until recently because of its great toxicity and instability. Mapharsen is an example of an effective form of arsenoxide with low toxicity.

For a period of eighteen months we at the University of Pittsburgh have been studying the effects of phenarsine hydrochloride in established cases of syphilis.

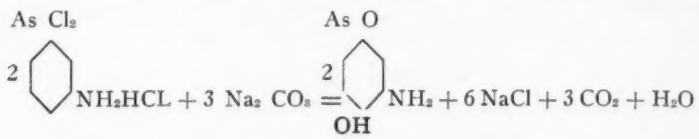
CHEMISTRY AND PHARMACOLOGY [1]

Two single dosage forms of phenarsine hydrochloride are available. The smaller dose contains 0.045 Gm. of 3-amino-4-hydroxyphenyldichlorarsine hydrochloride, which yields 0.0308 Gm. of the active principle, 3-amino-4-hydroxyphenylarsenoxide (arsenoxide). A dose of 0.04 Gm. of mapharsen yields exactly the same amount of active principle. The larger dose of phenarsine hydrochloride (0.068 Gm.) yields 0.047 Gm. of 3-amino-4-hydroxyphenylarsenoxide. This corresponds to 0.06 Gm. of mapharsen content of the active principle. Both phenarsine hydrochloride and mapharsen contain about 25 per cent trivalent arsenic. They do not contain inorganic arsenic.

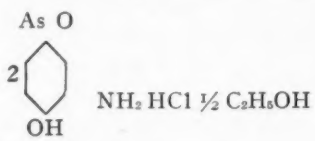
From the Department of Dermatology and Syphilology, University of Pittsburgh School of Medicine.

1. Data on chemistry and pharmacology are based on experiments by O. W. Barlow, M.D., PH.D., director of pharmacologic and biologic research, Winthrop Chemical Company, Inc.

Phenarsine hydrochloride in the dry form does not contain arsenoxide. Arsenoxide is formed by the chemical reaction which takes place in the ampule when distilled water is added according to the following equation:



The active material in mapharsen is arsenoxide hydrochloride hemialcoholate, which has the following structural formula:



On the addition of water to the ampule, a reaction takes place with the alkali present, in which the hydrochloric acid and alcohol in the molecule are split off, leaving arsenoxide. The fact that phenarsine hydrochloride in the dry form contains no arsenoxide is of importance from the standpoint of stability.

TOXICITY

Toxicity tests were carried out according to the standard National Institute of Health procedures in all respects. All doses were administered in 0.2 per cent concentration.

Of 77 rats receiving 14 mg. per kilogram intravenously the percentage of survivals was 96; of 62 rats receiving 16 mg. per kilogram the percentage surviving was 85.5; of 74 rats receiving 18 mg. per kilogram the percentage was 71; of 18 rats receiving 22 mg. per kilogram the percentage was 61. The toxicity of phenarsine hydrochloride does not differ materially from that of mapharsen.

THERAPEUTIC ACTIVITY

Experimental Study.—Curative tests on rats infected with Trypanosoma equiperdum were carried out according to the standard United States Public Health Service procedures. Of infected animals treated with 0.375 mg. per kilogram of phenarsine hydrochloride, 30 per cent survived the twenty-eight day observation period; of those receiving 0.4375 mg. per kilogram, 24 per cent; of those receiving 0.500 mg. per kilogram, 41 per cent, and of those receiving 0.625 mg. per kilogram, 61 per cent.

These results do not differ materially from those obtained with mapharsen.

The therapeutic index of phenarsine hydrochloride and of mapharsen is about 28.

Clinical Study.—Our investigation of phenarsine hydrochloride extended from January 1941 to July 1942. During this period 233 patients were given 2,581 intravenous injections of the drug. In addition to this number 26 patients were dropped from the series because of transfer or irregularity in attendance.

An untreated group of 4 patients with primary lesions in whom a diagnosis of syphilis was established by dark field examination received one intravenous injection of phenarsine hydrochloride and were immediately hospitalized to determine the effect of the drug on the disappearance of Spirochaeta pallida from the lesions. Dark field examinations were repeated at intervals until three negative results were obtained, and in all cases the spirochetes had disappeared from the lesions within twenty-four hours.

Cutaneous manifestations were rapidly cleared, and in the majority of cases they disappeared entirely in an average of fourteen days.

The following continuous course was used in all cases regardless of the stage of syphilis. A dose of phenarsine hydrochloride (0.068 Gm. for male and 0.04 Gm. for female patients) was given once weekly for six weeks followed by one dose (60 mg. of bismuth) weekly of an oil-soluble bismuth compound for six weeks. All patients with late stages of syphilis received supplementary medication with saturated solution of potassium iodide by mouth. Treatment was continuous without any intervals or rest periods.

In 1 female patient with secondary syphilis the drug (0.04 Gm.) was administered daily for twenty-five successive days. The secondary cutaneous lesions had disappeared at the end of ten days, and the patient tolerated the drug without any ill effects.

BY EFFECTS

In a small percentage of patients we encountered mild symptoms of nausea, gastrointestinal symptoms with vomiting, slight headache, pains in the arm when the drug was administered slowly, one nitritoid reaction and one Herxheimer reaction, characterized by overaccentuation of the lesions. Delayed reactions, such as encephalitis, changes in the optic nerve and renal, neuritic, purpuric or hemorrhagic encephalitis, were not observed. In no patients were there recurrences of lesions on the skin or mucous membranes after medication was instituted.

The question of depression of the hemopoietic system was considered. Complete studies of the blood were made, and in none of these did we see evidence of granulocytopenia or anemia.

Routine urinalyses were made in all cases prior to each injection of phenarsine hydrochloride or bismuth. At no time was treatment discontinued because of abnormal urinary findings or because of intolerance to the drug. In a few cases, when the patient complained of nausea or vomiting, the dosage was cut in half, and the drug was then well tolerated.

COMMENT

As this is a preliminary study and as we feel that conclusive results cannot be computed in the treatment of syphilis in such a brief period of time, we are not reporting any final results.

However, we do feel, from the information we have derived so far in this preliminary study, that phenarsine hydrochloride may prove more stable than and, further, that it compares favorably with, as far as administration, toxicity and early reports are concerned, other drugs which are now available on the market and which depend for their efficacy on arsenoxide.

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FUNGOUS INFECTIONS OF THE FEET TREATED WITH A CAMPHOR-PHENOL MIXTURE

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The purpose of our study was to determine the value of a camphor-phenol mixture as a cure for ringworm infections of the feet.

Francis [1] wrote that he had used a combination of equal parts of camphor and phenol with success in the treatment of "athlete's foot," the term "athlete's foot" being interpreted as referring to any type of fungous infection of the feet. This preparation was later brought to the attention of the public in a popular monthly magazine.[2]

Scott [3] said: "An unexplained chemical reaction takes place between camphor and phenol, making the latter a relatively innocuous material."

Phenol has other interesting properties. It is made weaker by alcohol and glycerin. However, of the three—camphor, alcohol and glycerin—camphor weakens it most, glycerin next and alcohol least.

The fungicidal effectiveness of equal parts of camphor and phenol was compared with that of an alcoholic solution of 2 per cent iodine, 5 per cent benzoic acid and 3 per cent salicylic acid, which will be designated hereafter as the alcohol solution.

For the clinical study, a group of 85 naval aviation students suffering from fungous infections of the feet were selected at random. They were grouped according to the clinical appearance of the lesions at the time of the initial examination. Of these, 52 (62 per cent) showed only a scaling and peeling about the toes; 15 (18 per cent) had fissures and maceration between the toes, and 18 (21 per cent) had varying degrees of vesiculation and erythema. The last two groups complained

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The opinions or assertions contained herein are the private ones of the writers and are not to be construed as official or reflecting the views of the Navy Department or the Naval service at large.

1. Francis, E.: Phenol-Camphor for "Athlete's Foot," J. A. M. A. **117**:1973 (Dec. 6) 1941.

2. DeKruif, P.: A Working Cure for Athlete's Foot, Reader's Digest **40**: 46 (May) 1942.

3. Scott, A.: Personal communication to the authors.

of discomfort (tingling, burning and tenseness). Fungous infection of the toe nails was present in 4 (5 per cent).

Before the camphor-phenol mixture was used as a remedy for ring worm, it was applied to the flexor surfaces of the forearms of 10 subjects daily for one week. There were no untoward reactions. In each test case there was an immediate erythema, which subsided within fifteen minutes.

In the aforementioned groups without regard to clinical differences, the camphor-phenol mixture was applied to the right foot and toes while the alcohol solution was painted on the left foot in like manner.

With the camphor-phenol mixture the patients noticed first a feeling of tingling followed by a prolonged sensation of anesthesia ("like the foot was asleep"). This reaction was comforting to those with fissures for about four hours, and then the discomfort reappeared.

Both medicaments brought about exfoliation between the toes in three days. For the group of 52 with peeling the preparations were equally effective, and no untoward reactions were noted from the camphor-phenol mixture. However, after cessation of treatment for one week cultures of material from feet under each form of treatment showed growth; this indicates that the camphor-phenol mixture does not cure fungous infection after one week of daily applications in contrast to the statement of DeKruif [2] that it does. In the group of 15 (18 per cent) with fissures and maceration there was short-lived relief from painful fissures with the camphor-phenol mixture. After three days of treatment it became apparent that this mixture did not promote healing and other treatment became necessary. In 2 cases the fissures became deeper and more painful. For this type of infection the camphor-phenol mixture should not be used. The alcohol solution is also contraindicated. Mild soothing treatment should be prescribed.

For the care of the 18 (21 per cent) with vesiculation, the camphor-phenol mixture offered no benefit and some harm. The blisters in 7 cases continued to enlarge. Dissemination of small blisters was not stopped or curbed by the medication. In 3 patients extensive toxic eruptions of the hands developed while they were undergoing this treatment. One other patient had a mild toxic erythema (swelling, redness and tenseness) of the hands, which subsided within twenty-four hours after application of the camphor-phenol mixture was stopped and use of boric acid soaks was begun. In no case did this mixture cut short the duration of the vesicular stage.

In 3 patients with tinea versicolor the camphor-phenol mixture was as beneficial as the alcoholic solution; however, all 3 complained of the unpleasant odor of the medicament, as did their companions and classmates.

The camphor-phenol mixture proved to be a primary irritant in the groins and perianal region. All of the 5 patients who used it complained

of excessive burning. Two of the 5 had redness and edema followed in three days by rawness and oozing. They objected to further treatment with this mixture, and the alcoholic solution was used later without producing the aforementioned symptoms.

SUMMARY AND CONCLUSIONS

In a clinical study of the effect of a camphor-phenol mixture in the treatment of fungous infections of the feet in 85 young men, we have come to the following conclusions:

The camphor-phenol mixture we used is not a cure for fungous infections of the feet.

It is not beneficial and may be harmful in the vesicular types of fungous infections.

It may retard the healing of fissures.

It should not be used in the groins or perianal region.

Patients object to its odor after a few days.

The successful treatment [4] of fungous infections cannot be based on one specific substance at present. Methods of treatment and agents to be used must be altered to combat the various clinical manifestations.[5]

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4. Andrews, G. C.: Diseases of the Skin for Practitioners and Students, ed. 2, Philadelphia, W. B. Saunders Company, 1938, p. 299.

5. Wise, F., and Sulzberger, M. B.: Treatment of Fungous Infections, in Yearbook of Dermatology and Syphilology, Chicago, Year Book Publishers, Inc., 1938, p. 7.

CONTACT DERMATITIS DUE TO RESIN-FINISHED FACING IN COTTON UNDERWEAR

REPORT OF A CASE, WITH CONSIDERATION OF THE CAUSE, PATHOGENESIS AND RELATED PHENOMENA

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The case to be reported of hypersensitivity to a resin finish used in various fabrics was 1 of a group of 10 similar cases which were investigated by me during the past year. This instance was deemed worthy of separate report because the data collected shed light on the precise cause of the eruption, its pathogenesis and other related phenomena.

REPORT OF CASE

A man 65 years old was first seen on Jan. 27, 1942. About one and one-half years before this observation he had swelling of the penis and scrotum accompanied by a generalized eruption. This illness confined him to bed for nine days. The nature of the condition was not established at that time.

Three days before admission to the Skin and Cancer Unit he wore a new suit of unwashed cotton underwear. That evening he had sensations of itching. The following morning, despite the wearing of a pair of old, well tolerated pajamas, the penis and scrotum were swollen.

On examination these parts of the body showed a pronounced dermatitis with swelling and diffuse oozing. There was a bright red maculopapular eruption scattered irregularly along the midline of his hairy chest and abdomen; some of the lesions had a vesicular component, whereas others were centered by hair follicles.

A patch test was made with a piece of his cotton underwear, which had been washed in the interim. This was covered by two different types of adhesive tape. In forty-eight hours the skin was found to be unaffected by these materials, except that one tape showed some redness at its site.

Close examination of the underwear now revealed the presence of a narrow piece of facing on the under surface of the anterior aspect of the fabric, running along its midline. The following reactions to patch tests were obtained (read in forty-eight hours): facing material, an erythematovesicular reaction (at least 3 plus); washed pajamas, negative; undiluted partially purified abietic acid, 1 to 2 plus; undiluted lactone of 13-hydroxytetrahydroabietic acid, 1 to 2 plus; pure glycerin abietate, an erythematovesicular reaction (2 plus); two different specimens of wood rosin, one an FF grade and the other rich in phenolic bodies, each 1 to 2 plus; the abietic acid ester of pentaerythritol, an erythematovesicular reaction (about 2 plus); methyl abietate 50 per cent by volume in xylene, a pronounced erythematovesicular response (3 plus); a type of hydrogenated rosin, an erythemato-

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vesicular reaction (2 plus), and another type of hydrogenated rosin, an indefinite erythema (plus-minus). The remaining patches, which elicited no reactions, consisted of pure levopimaric acid, pure dehydroabietic acid, pure gum rosin, one specimen of wood rosin FF grade and dammar resin. At this time also (four days after the original patch was applied), the site of the adhesive tape which had previously shown some erythema had now become definitely vesicular, whereas the site of the other adhesive tape was still normal. At the same time a third type of adhesive tape caused a vesicular-edematous reaction.

Patch tests were then made with the facings of two other pairs of unwashed cotton underwear of the same grade, and these elicited vesicular reactions (3 to 4 plus). Tests were also made with methyl abietate in various dilutions, ranging from 100 per cent to 16 per cent by volume in xylene, and, while the responses to all these dilutions were positive, the intensity of the reactions diminished definitely as the concentration of the methyl abietate decreased. In addition, the skin was not affected by a commercial type of dehydrogenated rosin, consisting chiefly of dehydroabietic acid; this was the resinous component in the adhesive tape which had been well tolerated.

About two weeks later I obtained a sample of the resinous substance which caused the dermatitis. This is an "ester gum" made by esterifying abietic acid with a special type of alcohol. For convenience I shall call this the special ester gum. This was applied to one arm in the following concentrations: 32, 16, 6.4, 3.2 and 1.6 per cent by weight in xylene. The patient was watched carefully for signs of local irritation, and because itching occurred within five minutes these patches were removed; the sites showed only mild redness at the time. The same dilutions were then applied to the opposite arm, but this time the specimens were diluted with equal volumes of liquid petrolatum, the concentrations of the resin thus being reduced by approximately half. Since there was no inconvenience at the end of one-half hour, the patient was permitted to go home. On his return, in forty-eight hours, the reactions at all the sites were found to be intensely positive. The various concentrations of the special ester gum (approximate values) showed the following reactions: 16 per cent by weight in xylene and liquid petrolatum, an erythematovesicular and edematous reaction extending far beyond the original site of application (4 plus), 0.8 per cent by weight in the same solvents, an erythematovesicular reaction (about 3 plus), and the intermediate concentrations, effects in between these extremes. There was intense itching at all the sites.

On the opposite arm, where the special ester gum in xylene had been applied for only five minutes without the additional dilution with liquid petrolatum, there were even more intense reactions, and that portion of the limb was diffusely involved, with superimposed pronounced edema. The remarkable feature was the presence of bright red, irregularly scattered papules situated on the lower portion of the arm and on the corresponding forearm, especially the flexor aspect. These lesions, which resembled a "toxic erythema" or a "multiform erythema," did not undergo eczematous changes but retained their original appearance, with complete disappearance in about a week. There were no constitutional symptoms and no exacerbations at the sites of other patches or in the original eruption itself, the latter having regressed some two weeks after the cotton underwear was discarded.

COMMENT

1. *The Question of Group Hypersensitivity to Ester Gums.*—The term ester gum as used in the rosin industry is generally applied only to glycerin abietate, an ester formed by interaction of glycerin with the

abietic acid in rosin (wood or "gum"). However, numerous other ester gums are now available because of the use of other types of alcohols. Thus, in my case the following ester gums were employed in patch tests: methyl abietate, glycerin abietate, the abietic acid ester of pentaerythritol and the special ester gum. The chemical reaction of esterification does not proceed to absolute completion; hence some free abietic acid remains in the final product. This is designated by the acid number, which signifies the amount of potassium hydroxide in milligrams required to neutralize the free acid present in 1 Gm. of the ester gum. All ester gums therefore have an acid number, and this is generally low, in the neighborhood of 4 to 8.

In my case there was a variable, but definite, hypersensitivity to all four ester gums. The weakest reactions were obtained with undiluted specimens of glycerin abietate and of the abietic acid ester of pentaerythritol (solid substances). More intense reactions were given by methyl abietate (a viscous liquid) in various concentrations of xylene, and a still more pronounced cutaneous response was elicited by the special ester gum, even when the latter was in small concentration in both xylene and liquid petrolatum as the diluents. The evidence therefore indicated that the last-named substance was the cause of the dermatitis.

Analysis of the protocol in this paper reveals that the 2 plus reaction to the undiluted glycerin abietate could not be compared in intensity, form and course with that elicited by the resin-impregnated fabric in which the etiologic factor existed in a diluted state. Three days after the patches were removed, the reaction to glycerin abietate had practically faded, whereas that caused by the finished material was still present in its former intensity. Such comparisons must however, be made cautiously, because the physical state of the resinous substance in the fabric (presence of a wetting agent) is an important complicating factor. The view that glycerin abietate is the cause of this eruption is negated by the data which I have collected in 10 cases of this type of dermatitis.[1]

2. *The Question of Associated Hypersensitivity to Adhesive Tape.*—The occurrence of group reactions to various ester gums explains, in great part, the discordant opinions on the question of reactions to adhesive tape seen in these patients. Some observers[2] have found that all persons giving a positive reaction to a patch test with resin-

1. Keil, H.: Dermatitis Due to Resin-Finished Shorts and Fabrics: An Investigation of the Cause, Pathogenesis and Related Phenomena in Ten Cases, to be published.

2. Schwartz, L., and others: An Outbreak of Dermatitis from New Resin Fabric Finishes, J. A. M. A. **115**:906 (Sept. 14) 1940.

impregnated fabric or with the "oleoresinous" mixture used for finishing were also hypersensitive to adhesive tape; others, myself included,[3] have encountered cases in which this was not true. The data which I have collected indicate that this depends essentially on the composition of the tape. Thus, in the case recorded there were positive reactions to two types of adhesive tape, one eliciting an immediate and the other a delayed response. A third variety of tape, the composition of which was known to me, was well tolerated, and patch tests showed that the patient was not sensitive to its resinous ingredient, a commercial form of dehydroabietic acid. It may be postulated that the two types of adhesive tape which gave positive reactions probably contained some variety of ester gum.

To summarize: A positive reaction to a patch test with adhesive tape in these cases depends chiefly on two factors: (1) the presence of an ester gum in its composition and its concentration and physical state in the formula and (2) the degree of group hypersensitivity. There are some exceptions to the rule of group reactions, but the principles are similar. One point must be made clear. If, as in the case recorded, a 2 plus reaction is obtained with undiluted glycerin abietate, this does not necessarily mean that a piece of adhesive tape containing this ingredient will not be tolerated if applied to the skin for twenty-four hours. The concentration and physical state of this substance in the tape may be such that no clinical evidence of hypersensitivity is manifested. This is especially true of patients who have only a low grade of group hypersensitivity to glycerin abietate. In most instances, however, a positive reaction to this type of adhesive tape may be expected because group reactions to the ester gums are generally pronounced.

3. *The Question of Abietic Acid as the Etiologic Factor.*—Free abietic acid is found in relatively small amounts in all the ester gums used in my studies. In addition, a moderately positive reaction (1 to 2 plus) was elicited by undiluted partially purified abietic acid. On the other hand, negative responses were obtained with some specimens of rosin which are rich in this substance, such as gum rosin and a variety of wood rosin, FF grade. It may be noted that my specimen of partially purified abietic acid had changed in color from its original pure white to yellow, indicating the presence of oxidized products. It is possible, though precise proof is lacking, that the reaction to the abietic acid may have been caused by the oxidized portion. The intensity of this reaction was much less than that shown by the facing material in which the resinous ingredient was present in a diluted state; moreover, three

3. Keil, H., and Bereston, E. S.: Dermatitis Due to a Transparent Adhesive Tape, Arch. Dermat. & Syph. **45**:1052 (June) 1942. Morse, J. L.: Dermatitis Venenata (Due to Underwear Shorts), ibid. **43**:719 (April) 1941.

days later the reaction to the partially purified abietic acid had disappeared, whereas that produced by the finished material was still intense. These observations therefore substantiated the conclusions reached by Neilson and Reiches [4] and Bereston and myself [3] that abietic acid was not the cause of the dermatitis due to shorts which were finished with the same "oleoresinous" finish.

It has been assumed [5] that sensitivity to rosin (composed chiefly of abietic acid) necessarily means that abietic acid is the sensitizing agent. That this is not true is shown conclusively by the observations which I was able to make in the following connection. In 1923 Beinhauer [6] reported a case of dermatitis of the hands due to a violin rosin. This was composed of several ingredients, but patch tests with only the dark wood rosin F elicited a pronounced positive reaction. Through Dr. Beinhauer, the two chief ingredients were recently sent to me; one was a dark wood rosin and the other a gum rosin, probably WW grade. Chemical tests showed that both contained abietic acid, yet only the wood rosin had produced a pronounced positive reaction when applied in a patch test. This difference in cutaneous response might have been attributed possibly to some difference in the physical state of the abietic acid in these rosins, a supposition which I believe is unlikely in this case. A better explanation was found in the results of a chemical test for phenolic bodies; the gum rosin gave a negative reaction, whereas the wood rosin was rich in them. The conclusions reached by me were: A. Since abietic acid was common to both rosins, the difference in concentration being negligible, it could not be the cause of the positive reaction to the patch test with the dark wood rosin. B. The probable cause was the content of phenolic bodies in the dark wood rosin.

4. *The Question of Primary Irritation and of Sensitization by Rosin and its Derivatives.*—A more complete discussion of this problem will be given in another publication. Summarized briefly, there is no substantial evidence that the various rosins used in my case are primary irritants. On the other hand, these substances have varying degrees of sensitizing power. Under present conditions of industrial use, abietic acid seems to be an uncommon sensitizer, glycerin abietate an occasional sensitizer and the special ester gum which caused the eruption in my case a fairly frequent sensitizer. A person sensitized to one type of rosin or its derivatives may become hypersensitive to other

4. Neilson, A. W., and Reiches, A. J.: Contact Dermatitis Due to Underwear: Observations in Fourteen Cases with Summary of Efforts to Discover the Cause, Arch. Dermat. & Syph. **44**:218 (Aug.) 1941.

5. Schwartz, L., in discussion on Morse, J. L.: Dermatitis Venenata (Due to Underwear Shorts), Arch. Dermat. & Syph. **43**:719 (April) 1941.

6. Beinhauer, L. G.: Resin Dermatitis: Report of Case, J. A. M. A. **81**: 13 (July 7) 1923.

varieties, but exceptions do occur. Group hypersensitivity is especially common among the ester gums, particularly when sensitization is produced by an ester gum applied to relatively large tracts of the body in a readily available physical state (increased penetration due to the use of wetting agents).

5. *Is Sensitivity to Rosin and Its Derivatives Enhanced by Xylene?*—The various dilutions of methyl abietate in xylene gave reactions showing that the effects of the ester gum depended on its concentration and not on the presence of the solvent. Similar studies with the special ester gum which was diluted with both xylene and liquid petrolatum appeared to substantiate this view. Other studies, which will not be described here, also showed that the presence of xylene and of other solvents exerted no special effect in the presence of many resinous substances eliciting positive reactions other than to weaken the cutaneous response by simple dilution.

6. *The Question of "Toxic Erythemas" in Association with this Dermatitis.*—In this hypersensitive patient there was sufficient local absorption of the special ester gum to produce a toxic erythema near the sites of greatest concentration. The simultaneous occurrence of epidermal hypersensitivity (eczematous reaction) and of vascular or possibly lymphatic hypersensitivity (toxic erythema) was therefore illustrated. The irregularity in distribution of the papular erythema and its confinement to the lower part of the arm and the corresponding forearm of the limb to which the special ester gum had been applied for only five minutes in fairly large concentration seemed to argue for lymphatic absorption rather than direct entrance into the blood stream; however, I am not certain of this. The observation sheds light on two points of interest: A. It explains why one sometimes sees a combination of eczematous or edematous reaction in the skin of the scrotum (anatomic attributes, points of contact, sweating, etc.), whereas the neighboring thighs or abdomen show lesions of a more deep-seated "toxic" type. B. The generalized multiform and urticarial lesions encountered in some instances as well as the constitutional symptoms may be explained as dependent on the degree of local absorption in an especially hypersensitive person. In other words, there may be encountered in some cases not only a local contact dermatitis but also evidence of local absorption, followed in cases of severe involvement by systemic absorption.

7. *Significance of the Incubation Period.*—The incubation period may be defined as the time elapsing between the first wearing of the fabric and the onset of local cutaneous manifestations. When precise data can be obtained, this is generally found to be of one of two types: (*a*) a long period, of from seven days to perhaps several weeks, and (*b*) a short period, of from one to three days.

A. The long period of incubation affords definite evidence that the resin finish was the actual sensitizer. It seems improbable that a preceding hypersensitivity to adhesive tape adequately explains these cases for at least two reasons. In the first place, in some instances I was able to ascertain that adhesive tape had been well tolerated on many previous occasions. Secondly, these fabrics generally cover large tracts of the body, so that even if one assumes that the fabrics had been washed before wearing there would remain a sufficient amount of resinous substance to elicit cutaneous manifestations if the patients were already sensitive to a group or related rosin. It is unlikely that the special ester gum in the finish was previously used in adhesive tapes, because it is a relatively new compound and its fairly low melting point militates against its use in such products.

B. A short incubation period (one to three days) indicates probably an already established hypersensitivity. Thus, in the case recorded, it is likely that the patient was sensitized one and one-half years before the present observation. It required but twelve hours to provoke a fresh attack, and the data indicated that both exposures involved the same ester gum. It is possible, however, that some patients falling in this general category may manifest an immediate cutaneous response to the special ester gum as a result of previous hypersensitivity to adhesive tape by virtue of the principle of group or related chemical reactions. This point needs substantiation before final acceptance.

SUMMARY

A case of contact dermatitis due to a resin-finished facing in cotton underwear is described. Investigations show that the cause is a special ester gum made from abietic acid and a special type of alcohol. There is no evidence to implicate either glycerin abietate or abietic acid in this case, as well as in others which I have studied.

The following problems are discussed briefly: (1) group hypersensitivity to various ester gums; (2) associated sensitivity to adhesive tapes; (3) abietic acid as the etiologic factor; (4) primary irritation and sensitization caused by rosin and its derivatives; (5) relation of xylene to the degree of sensitivity to rosin and its derivatives; (6) "toxic erythemas" and systemic symptoms in relation to this type of dermatitis, and (7) significance of the incubation period in these cases.

Dr. Louis Fieser provided me with some of the chemicals used in this study.

509 Madison Avenue.

Clinical Notes

ALOE VERA (JELLY LEEKS)

COLONEL M. THOMAS TCHOU, CHUNGKING, CHINA

I was born and raised in the town of Tzechow, which is at the foothills of the Tibetan Plateau and the Himalayan Range in western China. Like most boys, I preferred to fly kites, catch birds and plant flowers rather than to memorize the Confucian classics.

One day I caught a young bird, much like a vireo, freshly out of its nest. I put the bird in a wooden cage which had bars on one side only. Having raised two of the bars, I placed the cage on the ground near the tree in which the nest rested and waited in ambush. Finally the mother bird came to the cage with a worm to feed her fledgling. I cautiously sneaked up behind and pushed down the bars, thus capturing both the mother and her child, and took them home.

My first desire was to have a larger and better home for my protégés. Knowing the futility of asking either my grandmother or my mother for money, because it was against the Buddhist belief to keep live subjects in captivity, I decided to make a cage myself with strips of bamboo. In order to make holes in the horizontal girders through which the bars were to pass, I employed a hot iron rod heated in the burning coals of the kitchen stove. By holding one end with a piece of damp cloth, I was able to burn a series of well spaced holes with the red hot point of the rod. Accidentally the damp cloth slipped, and the thumb and the index finger of my right hand were burned. The burn was very painful, and blisters developed. At last I went to my ninth aunt, Narcissus, who was only a few years my senior and always sympathetic when I was in trouble. "Why don't you apply some jelly leek?" she exclaimed. It happened that she had a piece on her dresser, which she had picked that morning from one of the pots in the garden, for use on her hair. The jelly lubricated her luxuriant black hair and imparted a beautiful gloss. She split open a section of one leaf and applied the jelly side to my blisters. It had a wonderfully soothing effect—a marvelous relief! In a few days the sores were healed.

Thirty-eight years later, in 1939, I called on Dr. Harold N. Cole, of Cleveland, on the recommendation of my good friends Drs. A. C. Siddall and W. Frederick Bohn of Oberlin Ohio, for the treatment of an extensive ulceration on my right sole, which was the result of an overdose of radium received two and one-half years previously in China when I was suffering from a cutaneous ailment. Dr. Cole advised applying Aloe vera and kindly arranged for me to procure two leaves of the plant. I cannot describe my suprise when I opened the parcel and found two leaves of the "jelly leek" which I had known all these years! With rest in the hospital and application of the split leaves, once more my sores were healed completely.

O "East is East and West is West," and now the twain have met! In medicine, as in other fields, there are many things in common in East and West. Mutual benefit results from exchange. By combining discoveries and experiences, human life may yet be made better and happier.

ALOE VERA IN ORIENTAL DERMATOLOGY

H. N. Cole, M.D., and K. K. Chen, M.D., Cleveland

Only in the last few years have physicians in America been acquainted with the value of Aloe vera in the treatment of radio dermatitis and of certain chronic ulcerations.[1]

Colonel Tchou explained to one of us that jelly leek (Aloe vera) was a well known remedy to the Chinese medical man and to the Chinese household. Recourse was then had to the junior author for further information along this interesting line.

From examination of the most reliable treatises on Chinese materia medica it is believed that jelly leek is a local name for aloe in Tibet and its vicinity. The common name in China is *Lu Hui* (*Lu* means black and *Hui* deposits). The fresh plant is perhaps seldom used in China, but the jelly of the leaves is desiccated and sold in drug stores; thus it has its name.

There are, apparently, more than one species of Aloe which have been used in Chinese medicine. Thus, in Stuart's "Chinese Materia Medica"[2] it is described under the name "Alöe vulgaris." Besides its use internally, mention is made that: "It is now used mainly as a wash for eczematous skin affections, being combined with licorice for that purpose."

Apparently the same plant has been used in India for some time, as described by Chopra in his book "Indigenous Drugs of India":[3] "The uses of aloes, the common 'musabbar,' for external application on inflamed painful parts of the body and for causing purgation are too well-known in India to need any special comment. Its application in medicine dates back to the 4th century B.C."

According to the Chinese medical classics, aloe, or *Lu Hui,* has the following historical account:

During the Tang Dynasty, 618 to 905 A.D., it was advocated for the treatment of sinusitis by local application and for the reduction of fevers in children by internal use. A scholar named Liü Yu-hsi (772 to 842 A.D.) derived dramatic results by the application of the fresh leaf on his eczematous skin on his trip to Tibet. This was the only reference to use of the fresh leaf for cutaneous ailments.

During the Sung Dynasty, 960 to 1276 A.D., aloe was employed in the treatment of dental diseases and also of eczema by local application. It was used again in the form of a galenical preparation.

During the Ming Dynasty, 1368 to 1643 A.D., aloe was prescribed as a cathartic and an anthelminthic and also for the control of convulsions in children, all by internal administration.

The entire medical world is now well acquainted with the use of ephedrine, a drug employed by the Chinese physicians for thousands of years.

Here again with the use of Aloe vera, apparently oriental physicians as well as the laity have preceded their Western brethren by centuries at least.

From The Department of Dermatology and Syphilology, Western Reserve Medical School, Cleveland, and The Lilly Research Laboratories, Indianapolis.

1. Collins, C. E., and Collins, C.: Roentgen Dermatitis Treated with Fresh Whole Leaf of Aloe Vera, Am. J. Roentgenol. **33**:396 (March) 1935.

2. Stuart, G. A.: Chinese Materia Medica, Shanghai, American Presbyterian Mission Press, 1911, pp. 29-30.

3. Chopra, R. N.: Indigenous Drugs of India, Calcutta, India, The Art Press, 1933, pp. 57-58.

PITYRIASIS VERSICOLOR ON THE FACE OF AN INFANT

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The occurrence of pityriasis versicolor in infancy is a rare phenomenon, and it is even more unusual when it appears on the face. According to Fox [1] and Ormsby,[2] this disease is seldom seen in childhood, and when it does occur it is usually found in children who are approaching the age of puberty. A search of the literature does not reveal any similar report.

REPORT OF A CASE

D. H., a white boy aged 5 months, was referred to me by Dr. C. G. Hanson, of Cranford, N. J., because of an eruption on the nasal halves of both upper orbital margins. The patient's mother stated that they were first noticed as pinhead-sized yellowish macules when the child was 2 days old. Since that time they have become more numerous and some have coalesced to form superficial scaly macules about the size of a pea in diameter. At no time have the lesions regressed or disappeared; they have gradually assumed a brownish yellow hue. An abnormal tendency to perspire in these two symmetric locations has also been noticed by the mother and is the only possible cause for the appearance of the eruption in these locations.[2] The remainder of the skin on the body and scalp is free from pityriasis versicolor, seborrhea or eczema. There was an erythema in the diaper area, of recent origin. It was difficult to account for any contagion, other than a possible contact in the hospital, as the mother and father had had no similar lesions or achromia parasitica.

A few of the adherent yellow scales were carefully removed and cleared with 15 per cent potassium hydroxide. Microscopic examination of this preparation revealed the presence of numerous Malassezia furfur fungi scattered throughout. This was confirmed by the use of Wood's filter, which produced in the involved areas the characteristically brilliant golden yellow fluorescence of pityriasis versicolor.[3]

Summit Medical Group.

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1. Fox, H.: Diseases of the Skin in Infancy and Childhood, New York, D. Appleton and Company, 1930, p. 195.

2. Ormsby, O. S., in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1926, vol. 8, p. 92.

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Correspondence

SYNOVIAL LESIONS OF THE SKIN

To the Editor:—In the November 1942 issue of the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY, there appears an article, "Pathogenesis of Synovial Lesions of the Skin," by Drs. Alfred Eliassow and Samuel B. Frank. On page 693 is the following statement: "We have felt, therefore, that a better understanding of the problem could be obtained from a roentgenogram taken immediately after the injection of a contrast fluid into the lesion. A search of the literature does not reveal any observation made with this method."

I wish to call attention to an article, "Ganglion-X-Ray Study and Treatment," which I read in the section on Dermatology and Syphilology of the Southern Medical Association at the twenty-fifth annual meeting, New Orleans, Nov. 18, 1931. This article was published in the *Southern Medical Journal* (**25**:389 [April] 1932). I reported on 7 patients with ganglion or synovial lesions. Of the 7 patients, 5 received injections of iodized poppyseed oil prior to a roentgenographic examination.

The published summary of my study states in part: "An x-ray study of five cases of ganglia or synovial lesions offers some evidence that they develop from synovial membrane lining tendon sheaths and are connected with the sheath canals. Apparently they do not connect with the nearby joint cavities."

Roentgenograms accompanied the published article.

HOWARD HAILEY, M.D., Atlanta, Ga.

News and Comment

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

At the meeting of the American Board of Dermatology and Syphilology in Chicago on Dec. 4 and 5, 1942, 47 candidates were examined. Of these, 37 passed the examination, 1 failed and 9 were conditioned.

The candidates who were certified by the Board are the following: Major Carsten R. Anderson, Los Angeles; First Lieut. Eugene S. Bereston, Baltimore; Isadore Botvinick, Bethesda, Md.; Shirley S. Bowen, Houston, Texas; Clement E. Counter, Long Beach, Calif.; First Lieut. George H. Curtis, Cleveland; Joyle O. Dahl, Portland, Ore.; Lieut. (j. g.) Jack L. Derzavis, Washington, D. C.; Capt. James R. Drake, Mountainview, Calif.; First Lieut. Francis Elson, Huntington, N.Y.; Emanuel Gahan, New York; Major Earl A. Glicklich, Cincinnati; Harry C. Goldberg, Plainfield, N. J.; Solomon Goldman, New Brunswick, N. J.; Joseph Goodman, Boston; Capt. Samuel Greenberg, Brooklyn; Joseph B. Grindon Jr., St. Louis; Elmer R. Gross, Philadelphia; Capt. Malcolm W. Harrison, Houston, Texas; Louis Hutner, Jamaica, N. Y.; Capt. Francis J. Krugh, Homestead, Pa.; William R. Love, Cooksburg, Pa.; First Lieut. Paul Mapother, Louisville, Ky.; Joseph Markel, Bethesda, Md.; Irene A. Neuhauser, Chicago; Lieut. Walter R. Nickel, Washington, D. C.; Paul H. Power, Waco, Texas; Julius Raab, New York; Capt. Robert L. Rein, Brooklyn; First Lieut. Perry M. Sachs, New York; Ludwig Schwarzschild, New York; Robert A. Stewart, San Francisco; Albert Strickler, Philadelphia; Francis M. Thurmon, Boston; Morris Waisman, Chicago; David G. Welton, Charlotte, N. C., and First Lieut. Wendel M. Willett, Des Moines, Iowa.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

OSSEOUS SYPHILIS: CONFUSION IN DIAGNOSIS; A REPORT OF TWO CASES OF OSTEOMYELITIS OF LATE SYPHILIS. L. J. ALEXANDER and A. G. SCHOCH, Am. J. Syph., Gonor. & Ven. Dis. **26**:397 (July) 1942.

Two patients with unusual extensive syphilitic involvement of bone are reported on. Because of the unusual clinical findings, there were considerable delay and confusion in diagnosis. In 1 of them the delay in diagnosis was due to an unpardonable clinical error of recording a positive serologic reaction as negative.

One is justified, especially in the face of serologic evidence of syphilis, when osseous lesions present such a picture as to make diagnosis a problem, in suspecting syphilis and giving therapy for this disease a trial before attempting radical procedures.

THE TREATMENT OF SYPHILITIC PRIMARY OPTIC ATROPHY. J. E. MOORE, R. D. HAHN, A. C. WOODS and L. SLOAN, Am. J. Syph., Gonor. & Ven. Dis. **26**:407 (July) 1942.

This study consists of an evaluation of the results of treatment of 250 patients with syphilitic primary atrophy of the optic nerve seen in the syphilis clinic of the Johns Hopkins Hospital and in the private practices of two of the authors from 1918 to 1940 inclusive.

Primary atrophy of the optic nerve was found to occur in at least 8 per cent of all patients with clinical evidence of acquired neurosyphilis. The cerebrospinal fluid was found to be normal in nearly 7 per cent of all cases.

A presumptive history of early syphilis was obtained for 59 per cent of the male patients and for only 8 per cent of the female patients. The incubation period of the disease varied widely, though the majority of patients had onset of symptoms during the second decade of their disease. Only 1.3 per cent of all patients had received adequate treatment for early syphilis.

Primary atrophy of the optic nerve occurred more than twice as frequently in tabes as in other types of neurosyphilis. In uncomplicated dementia paralytica it was found to be rare. Many patients, however, presented primary atrophy of the optic nerve and pupillary changes as the only clinical manifestations of neurosyphilis.

Blindness occurred in 28 per cent of untreated patients within one year of onset of symptoms, in 50 per cent within two years and in almost 65 per cent within three years. Six years after onset of symptoms 75 per cent of the patients were blind and less than 90 per cent were blind at twelve years. Patients not blind at the end of three years subsequently did well, even in the absence of treatment.

Routine antisyphilitic treatment with the trivalent arsenicals and bismuth compounds failed to alter significantly the spontaneous course of the untreated disease.

Subdural treatment by the Swift-Ellis technic should be abandoned. Its dubious value in an occasional patient is outweighed by a risk of sudden extinguishment of vision in about 10 per cent of those treated.

Fever therapy is the only efficacious method of treatment. If visual failure progresses in spite of fever therapy, no other form of therapy is likely to be of value. Since early diagnosis is often possible only by routine determination of the visual fields, fundi and visual acuity, this procedure is recommended as a routine supplement to the clinical and laboratory examinations for all patients with

neurosyphilis. Only by early diagnosis and the immediate induction of malaria (fever therapy) is there any hope of arresting the most fulminating conditions.

Three of the authors' patients were subjected to an intracranial exploration. In none of these was adhesive optochiasmal arachnoiditis found at operation, and in none was there any beneficial or deleterious effect from the operation.

THE DIAGNOSIS OF LYMPHOGRANULOMA VENEREUM: AN EVALUATION OF A VIRUS ANTIGEN (LYGRANUM) PREPARED FROM CULTURE ON CHICK EMBRYO. S. J. AXELROD, Am. J. Syph., Gonor. & Ven. Dis. **26**:474 (July) 1942.

A virus antigen made from a suspension of the virus of lymphogranuloma venereum cultivated in the yolk sac of the chick embryo (lygranum) used for intradermal tests gives results consistent with the history or the clinical findings, or both, in a high percentage of cases. Administration of sulfanilamide in cases of the anorectal form of lymphogranuloma venereum may cause disappearance of the specific cutaneous sensitivity found in this disease. In 4 cases studied the author was unable to demonstrate either intrauterine infection with the virus of lymphogranuloma venereum or transplacental transmission of antibodies to the Frei antigen as determined by intradermal tests.

ANTHIOMALINE: A FURTHER EVALUATION OF ITS EFFECT IN LYMPHOGRANULOMA VENEREUM. B. SHAFFER, Am. J. Syph., Gonor. & Ven. Dis. **26**:489 (July) 1942.

Anthiomaline (lithium antimoniothiomalate), originally introduced by Sezary, Bolgert and Joseph in 1935, proved to be a satisfactory drug in the treatment of 33 patients with lymphogranuloma venereum, particularly the inguinal syndrome.

The author suggests that at times the alternate, or even concomitant, use of both anthiomaline and sulfanilamide might be efficacious when either alone might fail in the treatment of the anogenital syndrome of lymphogranuloma venereum.

REUTER, Milwaukee.

INDUSTRIAL ILLNESS DUE TO TETRYL. LEON J. WITKOWSKI, CARL N. FISCHER and HOWARD D. MURDOCK, J. A. M. A. **119**:1406 (Aug. 22) 1942.

Tetryl, or trinitrophenylmethylnitramine, is similar to trinitrotoluene (TNT) and is being produced as a military propellant. Employees handling tetryl powder often get a dermatitis.

In a study of 1,258 workers affected by tetryl, the presenting symptom in 944 of them was a dermatitis. Tetryl dermatitis most commonly occurs on the face, particularly in the circumocular region and on the lateral surfaces of the neck and less frequently in the cubital fossae and on the dorsal portions of the forearms. The dermatitis generally occurs between the second and the third week of exposure, and the first subjective complaint is that of itching or burning of the affected parts. The dermatitis appears as an erythematous area associated with varying amounts of edema. Epistaxis is a common and early complaint, occurring most frequently in the early waking hours. On examination, the bleeding points could be traced to small ulcerations of the nasal mucous membrane. Frequent complaints are sneezing, a nonproductive cough and pain in the chest. These symptoms generally occur during the first two weeks of exposure and are the frequent forerunner of tetryl dermatitis. Anorexia, mild nausea, flatulence and abdominal cramping are also common and occur in 10 per cent of all exposed workers.

Employees with mild tetryl dermatitis are allowed to continue their work. However, those with severe primary dermatitis are removed permanently from contact with tetryl.

Measures directed toward the prevention of tetryl illness were rotation of employees, assignment of open operations to rooms of small capacity, general cleanliness of employees, ventilation and temperature control and use of a protective cream for the skin. There was a decrease of approximately 50 per cent in

the weekly incidence of tetryl dermatitis when the protective cream was used. This cream was composed of 10 per cent zinc oxide and 1 to 2 per cent ferric oxide in a water-miscible casein base.

HENSCHEL, Denver.

ACTIVE SENSITIZATION IN HUMAN BEINGS WITH TRICHINA ANTIGEN. BESSIE BARON and MATTHEW BRUNNER, J. Allergy **13**:459 (July) 1942.

It has been previously observed that the injection of ascaris extract into non-sensitive persons produces a hypersensitivity of the skin. It was also found that these positive cutaneous reactions could be transferred to the skins of normal persons by the Prausnitz-Küstner technic. The authors undertook a study (1) to determine whether the cutaneous test doses of trichina antigen which are used as a diagnostic aid in determining trichinella infestation can sensitize the patients to this antigen, (2) to determine the nature of the immunologic mechanism involved and (3) because of the group relationship of Ascaris lumbricoides and Trichinella spiralis to observe the relationship of the sensitivities induced by these two antigens.

The study was made on three series of subjects, each consisting of 6 atopic patients, suffering from various allergic illnesses. In 6 of the 18 patients (33.3 per cent) decided hypersensitization developed after three to five injections, and 10 of the 18 patients (56 per cent) showed definite evidence of sensitivity by the ninth test dose.

The cutaneous reaction in sensitivity to Trichinella spiralis was found to be mediated by the atopic reagin and is transferable to the normal skin.

By means of passive transfer studies it was found that the common antigen is probably stronger in the ascaris than in the trichina extract, even though the trichina antigen transfers better on trichina serums.

From a practical point of view, the authors warn that the diagnostic value of trichina tests diminishes with repeated intracutaneous injections.

A VEGETABLE MILK SUBSTITUTE: TARO. BENJAMIN F. FEINGOLD, J. Allergy **13**:488 (July) 1942.

The author offers a recipe for a low cost formula based on taro (poyo meal) as a milk substitute for use in the diets of milk-sensitive children. The formula is easy to prepare, is palatable and may be offered from a bottle. Taro may also be used as a substitute for cereals or other starchy foods.

Ingredients:

(1) Poyo meal (taro)	20.0 Gm.	(5½ teaspoonfuls)
(2) Clear gelatin	4.0 Gm.	(1½ teaspoonfuls)
(3) Vegetable oil (olive, cottonseed, corn and sesame)	10.8 Gm.	(3 teaspoonfuls)
(4) Corn syrup	7.5 Gm.	(½ tablespoonful)
(5) Calcium gluconate	2.0 Gm.	(2 teaspoonfuls)
(6) Sodium chloride	2.4 Gm.	(½ teaspoonful)
(7) Water, to make	240 cc.	(8 ounces)

Preparation:

Weigh and mix the dry materials. Add the oil and mix to a paste. Add the corn syrup and water to make 240 cc., or 8 ounces. Cook over the direct flame for three minutes, stirring while cooking. Cool the mixture and restore to the original volume by the addition of water.

The protein, fat, carbohydrate and mineral content of the formula compares favorably with that of human or cow's milk. The caloric value per ounce is 26.67 calories. At the current market prices, a quart of the formula can be produced for 11 to 13 cents.

MENDELSOHN, New York.

FURTHER STUDIES IN ARSPHENAMINE HYPERSENSITIVENESS IN GUINEA PIGS: IV. VITAMIN A (CAROTENE) IN RELATION TO THE SENSITIZATION OF GUINEA PIGS TO OLD ARSPHENAMINE. WILHELM FREI, J. Invest. Dermat. **5**:117 (June) 1942.

Variations of the vitamin A (carotene) content of the fodder within a wide range had no significant influence on intracutaneous sensitization of guinea pigs to

old arsphenamine. The impression prevailed that animals given diets rich in vitamin A had on the average slightly stronger cutaneous responses to the sensitizing injection and the following injection than those on moderate or deficient doses.

DETERMINATION OF URINARY COPROPORPHYRIN I USING COMMERCIAL HEMATOPORPHYRIN AS A STANDARD. PAUL L. EWING and THEODORE CORNBLEET, J. Invest. Dermat. **5**:127 (June) 1942.

The authors advocate the adoption of a uniform standard for determinations of coproporphyrin so that the results of various investigators can be better correlated. Lack of uniformity in the values reported may be due to the use of different standards.

THIAMINE HYDROCHLORIDE—AN OBLIGATE WHEAL PRODUCING AGENT. FREDRICK KALZ, J. Invest. Dermat. **5**:135 (June) 1942.

Thiamine hydrochloride injected intradermally in 30 patients elicited in each one a reaction resembling that caused by histamine, consisting of an urticarial wheal with a surrounding erythema from 3 to 6 cm. in diameter. Thiamine hydrochloride seems to be an obligate wheal-producing substance, and therefore a positive reaction to an intradermal test with this drug is not conclusive proof of individual sensitivity.

URINARY EXCRETION OF NICOTINIC ACID IN VARIOUS DERMATOSES. SAMUEL I. GREENBERG, J. Invest. Dermat. **5**:139 (June) 1942.

The small number of determinations preclude drawing any definite conclusion. In the small number of dermatologic patients examined the urinary excretion of nicotinic acid was within normal limits.

THE EFFECTS OF PYRIDOXINE (VITAMIN B_6) ON PERSISTENT ADOLESCENT ACNE. NORMA JOLLIFFE, LOUIS A. ROSENBLUM and JOHN SAWHILL, J. Invest. Dermat. **5**:143 (June) 1942.

The authors state that the oral administration of pyridoxine (vitamin B_6) in amounts of 50 to 250 mg. daily in divided doses was effective in improving the skin of some patients with persistent postadolescent acne vulgaris.

BLUEFARB, Chicago.

CATARACT AND OTHER OCULAR CHANGES RESULTING FROM TRYPTOPHANE DEFICIENCY. J. R. TOTTER and P. L. DAY, J. Nutrition **24**:159 (Aug.) 1942.

The ocular manifestations observed by these authors in rats on a diet deficient in tryptophan were lenticular as well as corneal, but they were able to differentiate the cataract and keratitis or vascularization of the cornea from that described in riboflavin deficiency of the rat by Day and co-workers. The corneal lesions described could also be produced by a diet containing tryptophan but low in lysine. In addition to the ocular lesions, other changes associated with tryptophan deficiency of the rat were loss of weight, hunch back, unkempt appearance, alopecia, greasy hair and nervousness.

THE RELATION OF B VITAMINS AND DIETARY FAT TO THE LIPOTROPIC ACTION OF CHOLINE. R. W. ENGEL, J. Nutrition **24**:175 (Aug.) 1942.

In these experiments on rats, the effect of various vitamin deficiencies on the amount of fat in the liver was studied. The values for fat were expressed as per cent of ether extract on a dry weight basis. The diet used consisted of casein 18 per cent, sucrose 78 per cent and a salt mixture 4 per cent, supplemented with

the necessary vitamins in pure or synthetic form. The rats were weaned at 23 days of age and killed after three weeks.

It was found that 10 mg. of choline was the optimum daily dose but that in the presence of thiamine, riboflavin, calcium pantothenate and pyridoxine even 10 mg. or more of choline failed to prevent fatty livers. Addition of 3 mg. daily of inositol reduced the liver fat to the levels found in animals raised on a stock diet.

Fatty livers, like those originally reported on by Halliday resulting from pyridoxine deficiency, could be demonstrated only if the depletion was carried out eight weeks or more. The control animals receiving pyridoxine also had somewhat higher values of liver fat than animals on a stock diet, which may be due to the absence of inositol in the diet. In another series of experiments it could be shown that deficiency in unsaturated fatty acids (fat-free diet) increased the fat in the livers of the rats approximately 100 per cent over the normal average after eight weeks. This is further proof of the well known complementary action of pyridoxine and unsaturated fatty acids in the nutrition of the rat.

These experiments substantiate the findings of McHenry and Gavin on the lipotropic action of inositol, which is required in addition to choline for the maintenance of normal fat metabolism. While McHenry and others demonstrated the mechanism of choline and thiamine and inositol (or lipocaic) and biotin, Engel shows that other factors of the vitamin B complex and the unsaturated fatty acids are involved in the prevention of fatty liver of the rat. The author points out the parallelism of the lipotropic action of choline and inositol with the effect of these two substances on perosis of the chick, in which manganese has been shown to be an additional factor. [These studies on fat metabolism have important implications for psoriasis. In this disease the therapeutic action of lipocaic has been reported by Dragstedt, Becker and co-workers. Soya bean phosphatides, rich in inositol and choline, and wheat germ, as a good source of inositol and its esters, have been shown by Gross and Kesten to have therapeutic value against psoriasis and to reduce high serum cholesterol in human beings to normal values.—Abstracter.]

GROSS, New York.

KELOIDS AND THEIR TREATMENT. L. H. NASON, New England J. Med. **226**:883, 1942.

The cause of keloid is always traumatic in a person with a disposition to it. Such a person has a sort of fibroblastic diathesis, varying in intensity among races and persons. It is relatively scarce beyond the age of 50 and very rare in the aged. Of 50 children undergoing appendectomy, keloids developed in 28. There are regions where keloids rarely occur, for instance, the flexural creases. Nason explains this on the basis of constant change in the degree of tension and stress in those areas. Keloids occur more frequently where the skin is subject to relatively little motion and change. This possible etiologic factor should be thought of in the technic of surgical excision, which is described in detail. The highest per cent of satisfactory results was obtained by surgical excision followed by irradiation within three to five days.

AUROTHERAPY IN LUPUS ERYTHEMATOSUS: A STUDY BASED ON A FURTHER EXPERIENCE OF FOURTEEN YEARS. P. E. BECHET, New York State J. Med. **42**:609, 1942.

Bechet discusses gold therapy for lupus erythematosus after an experience of fourteen years and concludes that it is still the most efficacious treatment. It should never be used for acute lupus erythematosus disseminatus or in cases in which there is associated pulmonary tuberculosis. During treatment with a gold compound exposure to sunlight should be avoided. Doses should be started at 5 mg. and raised at weekly intervals to 10, 25 or 50 mg., this dose to be exceeded only in exceptional cases.

THE TREATMENT OF HYPERTRICHOSIS BY ELECTROCOAGULATION. C. LERNER, New York State J. Med. **42**:879, 1942.

Lerner has used electrocoagulation to remove superfluous hair in 103 cases. He recommends this method in preference to electrolysis because it is rapid and causes less pain and less scarring.

ARGYRIA CONFUSED WITH HEART DISEASE. S. A. LEVINE and J. A. SMITH, New England J. Med. **226**:682, 1942.

Levine and Smith report 5 instructive cases in which families worried about their children kept in bed for congenital heart disease, while the gray discoloration of the skin, mucous membranes and nails was argyria, due to the still popular use of silver preparations in the form of nose drops.

ERYTHEMA NODOSUM. M. H. POPPEL and A. M. MELAMED, New England J. Med. **227**:325, 1942.

In the department of radiology of Mount Sinai Hospital, New York, Poppel and Melamed reviewed 88 cases in which a diagnosis of erythema nodosum was made. In 4 cases the disease was associated with tuberculosis, in 7 with rheumatic heart disease, in 49 with grip, in 6 with ulcerative colitis, in 28 with arthralgia, in 2 with ingestion of a drug and in 4 with a past history of syphilis. Of 44 cases in which a tuberculin test was made, in 33 a positive reaction was elicited. Biopsies were made in 10 cases. Epithelioid cells were seen but no tubercle bacilli. In 14 of 56 available roentgenograms of the chest pulmonary changes or enlargement of intrathoracic lymph nodes was found.

MODERN TREATMENT OF SKIN CANCER. G. C. ANDREWS and M. C. BARNES, New York State J. Med. **42**:986, 1942.

Andrews and Barnes advise discarding of the biopsy punch, which they call an objectionable, outmoded instrument that conflicts with the tenets of good plastic surgery. They are in favor of using the scalpel in the direction of the lines of tension of the skin. For treatment of squamous cell epithelioma surgical excision is advised, and for basal cell epithelioma, roentgen therapy. Radium treatment in their clinic has been largely discarded. However, for squamous cell epithelioma of the nose, on account of the location, they advise roentgen therapy. Valuable details of dosage and technic are given. RONCHESE, Providence, R. I.

RESULTS OF IRRADIATION TREATMENT OF CANCER OF THE LIP: ANALYSIS OF 636 CASES FROM 1926-1936. B. F. SCHREINER and C. J. CHRISTY, Radiology **39**:293 (Sept.) 1942.

A series of 636 patients with cancer of the lip treated at the State Institute for the Study of Malignant Diseases in Buffalo between 1926 and 1936 with roentgen rays and radium is analyzed by the authors. All proved to have squamous cell carcinomas. Cancer of the lip occurred 38 times more frequently in men than in women and 29 times more frequently on the lower lip than on the upper lip. The disease was most frequently found between the ages of 50 and 80.

There were only 15 cases of leukoplakia. Keratoses preceded cancer in 197 cases. In most of the cases the lesion was treated with medium voltage unfiltered roentgen rays by the single large dose method. Some were treated by interstitial radium needles or seeds and others by external irradiation with the 4 Gm. radium pack.

The absolute cure rate for the total series, which included many cases of metastases to the cervical glands, was 58.9 per cent. CIPOLLARO, New York.

ASPECTS OF ALLERGY ASSOCIATED WITH NEUROSYPHILIS. EDUARDO BUENTELLO, Arch. de neurol. y psyquiat. de Mexico **4**:79 (July-Aug.) 1941.

Buentello proposes to answer several questions relative to the apparent discrepancy between the clinical symptoms and the serologic reactions encountered in cases of neurosyphilis. Statistics on the subject are cited from both the French and the German literature: Dujardin and Vermeylen reported 2 cases of typical dementia paralytica confirmed at autopsy but with negative serologic reactions. Ahronheim reported 443 cases of neurosyphilis, in 59 of which the serologic reaction of the spinal fluid was negative. Included in this group were 170 cases of tabes dorsalis, in 34 of which the fluid was normal, and 124 cases of meningomyelitis, in 25 of which the fluid was normal. The author adds 8 cases of neurosyphilis with typical clinical manifestations but with negative serologic reactions of the spinal fluid.

Emphasis is placed on various external factors capable of altering the serologic reactions without changing the course of the clinical symptoms. Specific medication of acute infectious diseases is able to modify and negativize the spinal fluid during the progress of the disease but may not prevent the appearance of symptoms. The questions of the role of allergy and transient anallergic phases are discussed in the light of their relation to positive or negative serologic curves and certain forms of neurosyphilis. Tabes dorsalis and dementia paralytica are considered to be anallergic phases that may be converted to an allergic phase by malaria therapy. The cutaneous lesions of the secondary stage of syphilis constitute a good system of reticuloendothelial defense that seems to favor the development of allergy and impede the development of tabes or dementia paralytica. The author concludes that spontaneous immunization is the direct result of the cutaneous rash; therefore therapy should not be started until after the development of the rash. If this is slight or does not appear, actinotherapy or other irritative measures should be employed.

MARSH, Los Angeles [ARCH. NEUROL. & PSYCHIAT.].

Society Transactions

CHICAGO DERMATOLOGICAL SOCIETY

UDO J. WILE, M.D., *President*

MICHAEL H. EBERT, M.D., *Secretary*

April 15, 1942

Unilateral Acrodermatitis Chronica Atrophicans: Avitaminosis. Presented by DR. HERBERT RATTNER.

Mrs. F. W., aged 59, reported to the dermatologic department of Mandel Clinic two weeks ago because of dermatitis of the eyelids. Examination showed also a smooth, bright red tongue, perlèche and a pitting edema of the legs. The skin of the dorsum of the left hand and forearm was atrophic. The underlying vessels showed through the skin. The surface was mottled with macular pigmented lesions, and scattered over the left forearm there were sharply outlined coin-sized erythematous and eczematous patches. There were areas with keratotic plugs on the extensor surface of both elbows. The patient complained of a burning sensation of the soles.

Treatment consisted of a high vitamin diet and administration of yeast tablets.

She returned today with improvement in the perlèche and the stomatitis, but there was little change in the rest of the picture.

DISCUSSION

DR. OLIVER S. ORMSBY: The case is one of unilateral acrodermatitis chronica atrophicans in which there is probably a secondary avitaminosis, the latter condition having been improved with two weeks' treatment. The diagnosis of the presenter can be supported.

DR. UDO J. WILE, Ann Arbor, Mich.: In my experience acrodermatitis on one side is rare. Did the patient have a background of syphilis?

DR. OLIVER S. ORMSBY: I have encountered several cases of unilateral idiopathic atrophy in which there was a syphilitic background. I have a photograph in one of my publications of a patient with the disease on one leg. That patient had a background of syphilis. Unilateral examples of the disease, while rare, do occur occasionally; so one should be familiar with them.

DR. HERBERT RATTNER: The Wassermann reaction was negative.

A Case for Diagnosis (Dermatitis Repens?). Presented by DR. L. F. WEBER.

About two years ago Sister E., a 70 year old nun, noticed changes in her nails. She was a baker for many years until forced to retire because of these changes.

During the last two months pitting of several nails has occurred, consisting of small punctiform depressions. At about the same time the nail plates have become partially detached from the lateral grooves. Several of the fingers show a loss of the nail. The nail bed of the left thumb showed pustules one week ago. The periungual tissues are affected, with extension to the tip and palmar surface. The toe nails are normal. The inflammation and recurrent pustular formation have not responded to various therapeutic measures.

DISCUSSION

DR. LOUIS A. BRUNSTING, Rochester, Minn.: This case brings up the usual problem of a differential diagnosis between dermatitis repens, fungous infection,

recalcitrant pustular eruption and pustular psoriasis. Because of the character of the changes in the nails I should favor the last-named disease.

DR. HARRY R. FOERSTER, Milwaukee: My diagnosis was pustular psoriasis, though Dr. Weber informed me that the changes in the nails exhibited in this case were usually not observed with pustular psoriasis.

DR. FRANCIS E. SENEAR: I feel that a diagnosis of dermatitis repens is much more logical than one of psoriasis in spite of the character of the changes in the nails. It has been taught that pustular psoriasis is essentially a palmar disease, starting on the palmar surface and progressing, while acrodermatitis starts at the finger tips and extends upward, and the latter course is followed in this case. Furthermore, as Dr. Weber suggested, structural changes are common in acrodermatitis and unusual in pustular psoriasis. Dr. Ormsby has had much experience with dermatitis repens, and I should like to hear his opinion of this case.

DR. OLIVER S. ORMSBY: Dr. Mitchell and I had a patient with dermatitis repens whom we showed before this society for many years. I believe the present case is one of dermatitis repens.

DR. UDO J. WILE, Ann Arbor, Mich.: I should like to suggest a third possibility. I have seen in a few bakers and also in some women who have been putting up jams and preserves a severe form of paronychia apparently due to a yeast organism. It is not unlikely that this woman has had a paronychia in connection with her baking activities and that the loss of the nail is due to involvement of the nail bed of the same nature.

DR. EARLE R. PACE: Cultures for fungi were made months ago by Dr. Benedek. Nothing grew.

Ulceronodular Syphilis with Factitious Dermatitis. Presented by DR. MICHAEL H. EBERT.

M. T., a white woman aged 44, states that seven years ago a pimple developed on the right side of her nose. The condition increased in extent until now it involves the entire face, ears and anterior portion of the neck. She asserts that there has been no syphilitic infection in herself or in her family. No Wassermann test was ever made until her present admission to the Cook County Hospital. She has had no surgical or other destructive treatments, but she states that she has been continually picking the lesions and applying various antiseptics. There is no history of tuberculosis in the patient or her family. She has had two normal pregnancies, one ten and the other eleven years ago.

There is a diffuse gridion type of noncontractile scarring of the entire face, causing bilateral ectropion with partial loss of eyelashes. There are a few pea-sized nodules near the angle of the jaw. The ears are irregularly scarred. The neck is similarly involved except for the polycyclic border made up in places of pea-sized light brownish nodules. The right pupil is slightly larger than the left; both pupils react to light and in accommodation.

The urine and the blood were normal. The Wassermann and Kahn reactions were each 4 plus. Roentgenograms of the chest and head were normal. Chemical examination of the blood showed that it was normal. The reactions to tests with old tuberculin in dilutions of 1:10,000 and 1:100,000 were negative.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: I feel that dermatologists must become interested in and acquire a knowledge of psychosomatic medicine. The handling of patients who have neurogenic or psychogenic eruptions must be carried out with the utmost care. The mere recognition that a dermatitis is self inflicted is not in itself the removal of the underlying cause. The help of a good psychiatrist who has an interest in this field is necessary.

DR. UDO J. WILE, Ann Arbor, Mich.: I should like to ask Dr. Ebert whether syphilis was diagnosed early. The extensive scarring and destruction suggest it

was not properly diagnosed. Syphilids of this nature respond so readily to treatment that the extensive destruction here might readily have been avoided if her infection had been recognized and treated early.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: Most of the scarring in this case is from neurotic excoriations, which may be the result of a psychic complex related to syphilis.

Xanthoma Disseminatum. Presented by DR. DAVID KAHN (by invitation).

Mrs. F. W., aged 39, presented for Dr. S. W. Becker, is an American housewife of Russian-Jewish extraction. Yellowish nodules developed on the lower portion of her left eyelid, on the right temple, in the left axilla and on the right leg two years ago. She has frequency of urination and nocturia.

Eleven years ago the patient was treated for acne vulgaris and an infection due to Trichomonas vaginalis. At that time she had gaseous distress, frequent "heartburn" and constipation.

Examination of the skin revealed isolated small bright yellow papules on the lower eyelid, the right side of the face, the left anterior axillary line and the ventral surface of the right leg. The soft palate had a yellowish hue.

The results of cardiovascular examination were normal. The blood pressure was 114 systolic and 80 diastolic.

Examination of the fasting blood lipids gave the following results per hundred cubic centimeters: Total lipids, 1,075 mg.; phospholipid, 230 mg.; acetone-soluble lipids (free and combined cholesterol, neutral fat and fatty acid combined with cholesterol), 845 mg.; total cholesterol, 510 mg.; ester cholesterol, 330 mg.; free cholesterol, 180 mg.; cholesterol ester (ester cholesterol multiplied by 1.7), 560 mg., and neutral fat, 105 mg.

The result of a dextrose tolerance test was normal. The urine was normal; the specific gravity was 1.009. The complete blood count was normal except for 7 per cent monocytes and 8 per cent eosinophils in 6,900 leukocytes. The Kolmer and Kahn reactions of the blood serum were negative. The basal metabolic rate was —11 per cent; one year ago it was —15 per cent.

Histologic examination showed small collections of densely packed histiocytes, most of which had a foamy structure; some Touton giant cells were also present.

DISCUSSION

DR. CARL W. LAYMON, Minneapolis: In a case like this an attempt should be made to differentiate between the tuberous and the disseminate type of xanthoma. In this instance there was a hyperlipemia, which is not usually present in xanthoma disseminatum. To me this was an extremely odd case.

DR. THEODORE CORNBLEET: I think that the term disseminated was used here not as a term fitting into the newer classification of the xanthomatoses, in which the disseminated form suggests, for instance, a normal cholesterol level, but more as a descriptive adjective indicating that the eruption was disseminated on the skin. This woman had a tremendous amount of lipids in the blood, and yet the skin showed few changes. Many subjects with such decided changes in the blood lipids eventually show some changes in their blood vessels; these may produce accidents, often suddenly and early in life. The liver in this patient probably is not involved, because there are no yellow ribbons along the folds of the palms and soles. My associates and I have been doing some work on the lipids of the blood in this type of disturbance and find that the cholesterol level of the blood runs more or less parallel to the amount of fat in the blood stream. This type of patient can have almost unbelievable amounts of cholesterol in the blood without there being precipitation. We feel that the cholesterol is dissolved in the fat and is carried as a passive factor. Another observation we have made is that there is a relationship of phospholipids with the cholesterol lipids. As some authors have shown, in this disease there appears to be a disturbance in their ratio. Under some circumstances phosphates and phospholipids can produce at least a partial absorption of xanthomatous depots.

DR. UDO J. WILE, Ann Arbor, Mich.: I should like to endorse what Dr. Cornbleet has just said. Dr. Arthur Curtis, my associate, is much interested in blood chemistry and particularly in the chemistry of lipids. During the past several months I have noted a striking coincidence of high values for blood fat in patients who have xanthoma of the eyelid and a not infrequent coincidence of hypertensive disease. The latter is even found in younger persons. The association of xanthoma of the eyelid with the cardiovascular damage is more than coincidental.

DR. JAMES H. MITCHELL: Does reduction of the intake of fat have any influence on the disease?

DR. UDO J. WILE, Ann Arbor, Mich.: Continued reduction of the intake of fat does not necessarily influence the course of the disseminated xanthomas. One may consider resolution of xanthomatous lesions in many cases as due to a sharp reduction in the calories, but this reduction may actually have a relative increase of fats over carbohydrates and proteins.

DR. S. W. BECKER: I think it will be necessary to study a large number of patients before one will be able to place the problem of xanthoma on a more tangible basis. Bloch was of the opinion that the chief observation in his patients was the imbalance which he found in the blood lipids. Here is a patient the results of whose laboratory studies do not conform to those of other patients. It may be that a large series of patients will have to be studied before a real picture of the various clinical factors as far as the underlying metabolic disturbance is concerned can be obtained.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: I should like to hear from Dr. Becker in regard to the present status of lipocaic in the treatment of this disease.

DR. S. W. BECKER: Lipocaic has been given to a few patients with xanthoma, almost universally with a reduction in the fat lipids. This patient has been treated with lipocaic for a few days, and this detailed examination will be repeated in a few weeks. There is some evidence that lipocaic may be of benefit to persons with diabetes who have these various changes in the lipids. In other words, even though patients with severe diabetes are kept alive by insulin, in many of them sclerotic or fatty changes develop in the vessels. It is hoped that lipocaic may help this particular complication.

DR. UDO J. WILE, Ann Arbor, Mich.: Do you not think there is a striking paradox between the small number of lesions and the striking changes in the blood fat?

DR. S. W. BECKER: I have found higher values for blood lipids than these in patients with psoriasis, but unfortunately I have not been able to make detailed studies on psoriatic patients, owing to lack of technical help. I assume that the upper limit of lipid content of the blood is around 750 mg., and I have obtained lipid values higher than 1,050 mg. in cases of psoriasis and of xanthoma.

Extensive Naevus Pigmentosus with Neuroma, Neurofibromatosis and Mesodermal Dysplasia. Presented by DR. E. P. LIEBERTHAL.

A girl aged 11 months was admitted to Michael Reese Hospital eight months ago for treatment of advanced malnutrition. Examination of the skin revealed a bathing trunk type of naevus pigmentosus and neurofibromatous lesions localized in certain areas. The nevus extends as a solid mass of slightly elevated black hyperpigmentation from the occipital region down over the shoulders and trunk to the lower part of the lumbar and sacral regions. From the latter regions it extends upward and anteriorly to encompass the upper half of the trunk leaving the midabdominal region free. Elevated, pea-sized to dime-sized and slightly larger, soft, button-like, brownish black, sharply outlined lesions are present in the posterior cervical regions, on the upper third of the arms posteriorly and on the upper half of the trunk. Similar lesions are present in the

lower midmammary areas. From the posterior cervical regions the nevus extends laterally and upward to involve the lobes of both ears and the zygomatic and submental areas and then extends downward on the anterior surface of the neck to join the solid mass of hyperpigmentation of the supraclavicular area and upper part of the chest. Long brown hairs are present in the hyperpigmented areas in the posterior cervical, zygomatic, submental and left frontal areas and on the upper third of the anterior and posterior surfaces of the arms. Satellite lesions, pea sized to dime sized and larger and varying from yellowish brown to dark brown, are present on the buttocks, the flexor and extensor surfaces of the thighs and legs, the dorsa of the feet and fingers of both hands and the palms and soles.

Histologic examination was done by Dr. Otto Saphir. The section was bound on one aspect by a thin layer of epidermis. The tissue immediately beneath this was composed of spindle-shaped cells with dense oval elliptic nuclei and long eosinophilic cytoplasmic processes which pursued parallel or intertwining courses. The nuclei varied in chromatin content, many being dense, and a few were in mitosis. In many fields these nuclei were in palisade arrangement. Cytoplasmic processes were obscure; the cells were fused and at intervals perforated by vascular channels or cutaneous appendages. These structures are characteristic of neurofibrosarcoma.

Widely spaced within this tissue were large brown pigment-laden cells. At one pole of the section a dense accumulation of these pigmented cells was intermingled with large mononuclear cells having clear cytoplasm and oval nuclei, whose delicate chromatin was uniformly distributed. These cells, arranged in clusters and cords, extended throughout the corium. These structures had the features of pigmented nevi. At the periphery of the section just beneath the epidermis were foci of young cartilage whose peripheral cells simulated in appearance those of the adjoining neurofibromatous tissue.

In one section nevus and neurofibromatous elements were more conspicuously intermingled and the cartilaginous plaques more deeply situated. In addition, the section showed misplaced adipose tissue, localized angiomatosis and mucous connective tissue with myxoblasts.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: A speaker before the Academy of Dermatology and Syphilology in New York made a statement about this type of lesion. He said that after years of observation in cases of extensive nevi he had found that these tissues are subject to development of cancer and other neoplasms later. It is surprising how persons with extensive nevi are candidates for another type of cancer in later life.

DR. UDO J. WILE, Ann Arbor, Mich.: Last month's discussion centered around the potential malignancy of large hairy nevi. The members will doubtless recall the 3 patients presented at this meeting with melanoblastomas arising from hairy nevi.

DR. MAX S. WIEN: I saw this patient when I first entered the service at Michael Reese Hospital and thought she had a bathing trunk nevus. Then I came across the report by Wilcox in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY in which melanosis of the central nervous system was found in addition to the cutaneous involvement. Netherton described rapid metastases to the brain and spinal cord which were found. He pointed out that in cases of this type one must think of future involvement of the spinal cord and rapid metastases.

DR. H. E. MICHELSON, Minneapolis: Every patient with this condition should be treated by excision and plastic surgery regardless of the size, extent and duration of the nevus.

DR. S. W. BECKER: I studied these sections, and I do not believe that they confirm the clinical diagnosis of neurofibromatosis. They show many nevus cells and are unique in that many of them contain cartilage, but the tumor tissue would fall in the class of what Masson called schwannoma, or neurinoma. In only one section was there a suggestion of Recklinghausen's neurofibromatosis.

DR. E. P. LIEBERTHAL: I realize that I should have made roentgenograms of the skull and long bones, which should be done in every case of suspected Recklinghausen's disease.

Trophic Ulcers Resembling Condylomas. Presented by DR. DAVID V. OMENS, DR. HAROLD D. OMENS (by invitation) and DR. C. E. KEMP (by invitation).

L. P., a girl aged 5 years, presents an eruption on the genitals composed of elevated, flat-topped papules, with maceration. She was born with a spina bifida, which was repaired ten weeks after birth.

DISCUSSION

DR. MINNIE O. PERLSTEIN: This patient was operated on for meningocele at about 6 or 7 weeks of age and had a complete paralysis and anesthesia from the level of the umbilicus to the knees, associated with recurrent appearance of ulcers in these areas. About two years ago she first appeared at the neurologic clinic of Cook County Children's Hospital. At that time the largest ulcer was 1¼ inches (3 cm.) deep. She had no bladder or bowel control. She was sent to the neurologic clinic because of behavior disturbances. She would not play or associate with other children because she was ashamed. She was given a bromide, and in a week there was bladder control, but bromoderma followed and administration of this medication was stopped. The area of anesthesia decreased to the saddle areas. The large lesions cleared. Two or three months ago these recurrent herpetic lesions developed which were small and painful. The neurologists believe that the child is getting a regeneration of the nerve and that the herpetic lesions are due to some irritation of the ganglion. For two or three months before the development of the herpetic lesions the child was taking thiamine chloride. The paresthesia is improving.

DR. DAVID V. OMENS: I have observed this child for the past four weeks. I find she still has a paralysis of the bladder and an anesthesia involving the saddle areas. When I first saw her she had the large lesion that Dr. Perlstein described. I thought it was due to the fact that salves were being used. I stopped that and put on a dry dusting powder, and her condition has been progressing right along.

Subcutaneous Fat Necrosis of the Newborn. Presented by DR. DAVID V. OMENS, DR. HAROLD D. OMENS (by invitation) and DR. C. E. KEMP (by invitation).

L. C., a Negro girl aged 2 months, presents a patchy infiltration of the subcutaneous tissue on the left side of the body, on the left arm and on the lower extremities in the form of variable-sized plaques and nodules. The initial lesion on the left arm is undergoing softening and liquefaction, while the others are undergoing involution.

This eruption began two weeks after birth. There was a breech presentation after a prolonged and difficult labor, and the baby weighed 9½ pounds (4,309 Gm.). She is well nourished, and there has been no elevation of temperature at any time.

Examination of the blood showed 66 per cent hemoglobin; 3,600,000 erythrocytes; 15,200 leukocytes, with 39 per cent polymorphonuclear leukocytes, 58 per cent lymphocytes, 1 per cent eosinophils and 2 per cent monocytes; 161 mg. of cholesterol and 9 mg. of calcium per hundred cubic centimeters, and 6.25 per cent phosphorus.

Sclerema Neonatorum. Presented by DR. DAVID V. OMENS, DR. HAROLD D. OMENS (by invitation) and DR. C. E. KEMP (by invitation).

R. M., a Negro boy aged 4 weeks, was first seen at the age of 3 weeks, with several indurated areas of the skin of the back and posterior aspects of all four

extremities. The mother had first noticed the "lumps" about a week previously. There were no symptoms referable to this condition.

The child was born at full term and weighed 6 pounds 2¾ ounces (2,800 Gm.); labor was spontaneous, lasted eight hours and was not especially difficult. There is a family history of allergy.

DISCUSSION OF CASE OF SUBCUTANEOUS FAT NECROSIS OF NEWBORN AND CASE OF SCLEREMA NEONATORUM

DR. OLIVER S. ORMSBY: These conditions are rare. Subcutaneous fat necrosis of the newborn is a comparatively benign condition and is probably the same disease formerly described as scleroderma neonatorum. Nodules, plaques and deep-seated indurated areas develop shortly after birth; they undergo absorption and disappear in a few months. The favorable sites are the back and the buttocks, although they may occur on the extremities and the face. They are unaccompanied by constitutional symptoms. Sclerema neonatorum and edema neonatorum are grave conditions accompanied by constitutional symptoms and changes in the body temperature as a rule. In sclerema neonatorum the skin of the infant shortly after birth assumes a waxy hue and becomes leathery. The condition may become generalized. The palms and soles escape. The temperature is usually subnormal. Dyspnea, difficulty in swallowing and diarrhea are present. Death often ensues before the ninth day. Edema neonatorum begins shortly after birth and is characterized by a general edema, the skin being pallid, hard and cold. Drowsiness is present and increases as the disease progresses. Death occurs from pulmonary involvement or some intercurrent disorder. A certain proportion of the infants recover.

The first patient presents a good example of subcutaneous fat necrosis, a condition well described by Dr. Howard Fox a few years ago (ARCH. DERMAT. & SYPH. **27**:237 [Feb.] 1933). In the second case the duration is so short as to make a positive diagnosis difficult. Scleroderma of the newborn and subcutaneous fat necrosis are suggested.

DR. MINNIE O. PERLSTEIN: About nine months ago I saw a child who, after a stormy birth, was in an oxygen tent for twenty-four hours. Twenty-four hours later pneumonia developed and she was again put in an oxygen tent. She had all the signs of cerebral hemorrhage. Four days later generalized edema developed, with edema on the shoulders, buttocks and back. The edema started on the back and spread anteriorly, involving almost the entire body but not the face or the neck. This persisted for at least five or six days as a solid edema. Then gangrene of the buttock developed. There was an area of necrosis which sloughed out and left an ulcer 3 inches long and about 1½ inches wide (7.5 by 4 cm.). Four or five days later a similar lesion developed on one shoulder. The question came up as to whether the disease was fat necrosis, scleredema, scleroderma or sclerema. The child is now 9 months old and has recovered perfectly. Since the scars are soft and pliable, she had scleredema. I do not think the second baby presented has scleredema. It is probably scleroderma and will subside. The child is in perfectly good health. The other child has subcutaneous fat necrosis.

DR. F. W. LYNCH, St. Paul: Dr. Ormsby's discussion points out the satisfactory extent of the knowledge of the morphology of these diseases, but it indicates that dermatologic studies have failed to lead to any considerable knowledge of the physiological chemistry involved. Nothing will be gained by the presenting of such cases at meetings unless the members are in a position to perform microchemical analyses and similar detailed studies, as reported in a recent article by Luzzati and Hansen (*Proc. Soc. Exper. Biol. & Med.* **46**:325, 1941).

DR. THEODORE CORNBLEET: May I suggest that the infant's oxygen consumption be measured and the basal metabolism studied?

DR. M. H. EBERT: Why do you make that suggestion?

DR. THEODORE CORNBLEET: There might be a subnormal temperature, below a critical point, congealing abnormal, supersaturated fats. In a recent article one of the vitamins, probably vitamin E, was said to influence the character of fatty acids in subcutaneous fat.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: Scleredema of Buschke may occur in childhood, and I have observed 2 instances in babies. The disease developed after an acute infection of the respiratory tract, and the course was self limited with clearing in two or three years. In scleredema the chief points of attack are the neck, the face and the upper part of the trunk; the distal portions of the extremities are usually spared, and the disease has nothing in common with sclerema neonatorum.

Lichen Planus Involving the Palms. Presented by DR. THEODORE CORNBLEET and DR. H. C. SCHORR (by invitation).

J. A., a white man aged 63, has had a papular eruption for four months on both legs, both palms and the penis. There are lesions on the mucous membrane of the mouth. The patient had a similar eruption seven years ago, which lasted nine months. Itching is intense, and new papules continue to appear. Injections of a bismuth compound did not improve the eruption. A biopsy showed changes characteristic of lichen planus.

DISCUSSION

DR. OLIVER S. ORMSBY: Good therapeutic results might be obtained in this case with bismarsen.

DR. M. R. CARO: I have under treatment at present a patient with generalized lichen planus, with involvement of both the palms and the soles. The lesions on the hands and feet are healing as rapidly as the rest of the eruption.

DR. UDO J. WILE: I have seen lesions on the palms and soles. The late Dr. Arndt called attention to the fact that lichen planus could occur anywhere. He was one of the first to point out the not too infrequent lesions on the scalp, which were not looked for. Since then I have examined every patient with generalized lichen planus and found many with lesions on the scalp.

DR. THEODORE CORNBLEET: One of the teachings has been that the palms and soles as well as the head were not areas for the localization of lichen planus. Dr. Senear showed a patient several years ago with lichen planus around the eyelids. I have seen 2 or 3 patients with lichen planus on the palms.

A Case for Diagnosis (Epitheliomatosis and Devitalized Scar Tissue). Presented by DR. JAMES R. WEBSTER.

R. H., a white man aged 49, has had an eruption involving the face and neck for ten or eleven years. The lesions begin as papules or pustules, which usually become ulcerated and crusted and sometimes heal spontaneously after a period of months. In June 1940 biopsy of material from a lesion on the neck by Dr. Weller at Ann Arbor, Mich., showed a squamous cell epithelioma grade 1. Subsequently in another city he received roentgen treatment (a total of 5,040 r) at 200 kilovolts with moderate filtration to each side of the back of the neck in seven days. After this there was a painful reaction and the lesions did not heal. In October 1940 he again returned to Ann Arbor and was seen in the dermatologic clinic, at which time a diagnosis of radiodermatitis of the neck and cornifying squamous cell epithelioma of the face was made. Curettement and cauterization were advised for the facial lesion and application of a preparation of Aloe vera for the neck. The lesion on the neck still did not heal, and in June 1941 the ulcerated area was excised, after which healing was slow but eventually complete. In July a new lesion on the right side of the neck was treated by electrocoagulation, and the resulting ulcer is still present. About two months ago another new lesion appeared on the left side of the nucha and has somewhat increased in size. There is intense burning pain in these lesions but no subjective sensations elsewhere.

The patient's health, aside from "ulcers of the stomach" ten or fifteen years ago, is said to have been good, although he lost a great deal of weight two years ago, most of which he has regained. Sulfathiazole given for pneumonia last fall appeared to make the lesions much worse, and its local use has had no effect.

Over much of the nucha is a patchy, rather hypertrophic scarring, and there is also moderate vitiligo. There are no palpably enlarged or tender glands. In the right suboccipital region there is an irregularly round 25 cent piece–sized area of superficial ulceration with a rolled border (electrocoagulation in June 1941). To the left of the midline is an oval ulceration about 4 by 3 cm. in size with a well defined border over whose surface there are minute spots, at first glance appearing as pustules but on closer examination seen to be keratotic plugs. On the right side of the nose there is a small ulcerated lesion with a slightly elevated border of nine weeks' duration. At the left angle of the jaw in a previously existing scar there is a well defined ulceration with a slightly elevated threadlike border and a base of dirty granulation tissue. At the right angle of the mouth is a scar which at the time of the first examination, on March 6, 1942, showed an elevated inflammatory border, which has now entirely disappeared without treatment. In addition to these lesions, there are several scars on the face which are depressed and soft, all at the sites of preexisting lesions, some of which healed spontaneously and others apparently as the result of various types of treatment.

The urine was normal. A Kahn reaction was negative. A blood count was essentially normal.

At the first visit a smear from the surface of the recent lesion on the neck revealed the presence of a fungus which on culture was found to be an aspergillus. A subsequent culture revealed only a nonhemolytic Staphylococcus albus. A smear from the lower border of the specimen taken from the ulcerated area on the neck revealed no organisms or inclusion bodies.

A superficial specimen for biopsy from the margin of the lesion on the left side of the neck revealed a multicentric epidermal hyperplasia involving the squamous cells chiefly but exhibiting slight invasive tendency and relatively few mitotic figures. A few epithelial structures filled with stratum corneum were present.

A specimen from deeper within the ulcerated area showed practically no surface epithelium, there being some necrotic crusts in places. A few small strands of epithelium were seen in the midcorium. In the upper portions of the corium there were vascular dilatation and engorgement with moderate clumped perivascular round cell infiltration. The walls of the deeper blood vessels were considerably thickened. The connective tissue was rather coarse and homogenized, and there was clumping of the elastica. There were no blastomycetes, other organisms or inclusion bodies, in the sections.

The case is presented primarily for therapeutic suggestions in regard to the lesions on the neck.

DISCUSSION

Dr. Udo J. Wile, Ann Arbor, Mich.: This patient was seen in my clinic in 1940. At that time he stated that for six or seven years he had been troubled by boils on the back of the neck; these were opened and drained, but he was never free from them. In June 1940 biopsy of a specimen showed atypical hyperplasia of the epithelium and cornifying squamous epithelium with cells that were atypical. I think that in view of the man's history the pathologist made a shrewd diagnosis. The patient also had a chronic type of irritation. He gave a history of having received 5,000 r of roentgen rays. There were lesions on each side of the back of the neck. When I saw him I felt that he had a roentgen ray dermatitis and a roentgen ray cancer. He is presented with that diagnosis. One of the lesions was excised, with complete healing. The second and third lesions which appeared have not healed.

Dr. Harry R. Foerster, Milwaukee: This case emphasizes the danger in using any kind of destructive procedure on tissue that has been heavily irradiated. I believe that previous irradiation in this case had produced an endarteritis in small vessels in the areas of the original lesions and beyond the areas of recurrent lesions and that when electrodesiccation was employed the pathologic vascular bed could not compensate for the destructive and edematous

reaction. The result was trophic ulceration similar to what would have occurred if additional radiation therapy had been employed. I believe the entire field of vascular damage should be excised.

DR. JOHN F. MADDEN, St. Paul: It is my opinion that the ulcers all have one cause: I think that they may be self inflicted, because the site of the ulcer on the face did not have roentgen therapy. Before radical surgical excision is performed I think that some form of conservative therapy should be tried, such as occlusion dressings covering the lesions for at least a week.

DR. UDO J. WILE, Ann Arbor, Mich.: What have you in mind besides factitious dermatitis?

DR. JAMES R. WEBSTER: Apparently the patient had 5,040 r to this lesion in four treatments within a week. A lesion at the right angle of the mouth received a small amount of roentgen rays. None of the lesions except the ones on the back of the neck were painful, but he complains of a great deal of pain here.

DR. UDO J. WILE, Ann Arbor, Mich.: I do not think it was brought out in this patient's history that he had multiple epitheliomas to begin with.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: What was the original diagnosis?

DR. UDO J. WILE, Ann Arbor, Mich.: Before he consulted me he presented what I believed was a roentgen ray ulcer.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: There are no outstanding characteristics of actinodermatitis, and I suggest further conservative treatment.

DR. J. M. MCCUSKEY, Peoria, Ill.: I agree with Dr. Madden and Dr. Brunsting that this man's eruption is a dermatitis factitia. On the left cheek there is a finger nail–sized sharply defined shallow ulceration with a clean moist base. There are several similar-sized slightly depressed scars on the cheeks and sides of the neck, which are undoubtedly the remains of healed lesions similar to those just described. I made it a point to ask the patient about these scars. He stated he did not know of any preceding lesions on the cheeks or neck which could have produced these scars. Obviously any one who had lesions which caused enough destruction of tissue to produce scars of this size would have been aware of their presence.

DR. JAMES R. WEBSTER: I have only seen the man twice. He does not have the characteristics of a malingerer. He is well employed, and he has continued to work. He is driving back 150 or 200 miles this afternoon to be in time for work tomorrow morning, in spite of the fact that he came up for this meeting this morning. His history is rather complicated. I know that a tremendous amount of radiation was given two years ago. A diagnosis of epithelioma was made from the lesion on the neck at one time, of and at a later time Dr. Weller also made a diagnosis of the same type of lesion, for which he advised curettement and cautery. It cleared up satisfactorily. June 1940 5,040 r of roentgen rays at 2,000 kilovolts with 1 mm. of aluminum was administered in five doses. Following that there was a tremendous inflammatory reaction. Dr. Wile advised the use of Aloe vera leaf. Later the unhealed area was excised, in April 1941, nearly a year after the roentgen treatment. In July 1941 a lesion of some sort—I do not know what—was treated with electrocoagulation, and that has not healed. The lesion on the left side of the neck is of about two and one-half months' duration. It has been extremely painful. He is taking no opiates but controlling the pain with a combination of acetylsalicylic acid and aminopyrine. It is my impression that this is a breakdown in the tissue which has been devitalized by having the vascular bed damaged by roentgen treatment. My conclusion is the same as Dr. Harry Foerster's, that plastic surgical therapy should be performed. I shall, however, adopt the more conservative suggestions for the time being, as I do not wish to be overly drastic.

Obliterative Endarteritis with Onychomycosis (Monilia Albicans). Presented by DR. CLEVELAND WHITE.

M. O., a man aged 36, has had a swelling of the distal phalanx of the second finger of the right hand for one year with changes in the nail for three months. He has had an ulceration of the large toe of the right foot and of the little finger of the left hand intermittently for five and one-half years. He has had an ulceration of the right middle toe for three years. Several fingers have been amputated.

When he was first seen dermatologic examination revealed a heaped-up appearance of the nails with swelling of the right middle toe and a somewhat cyanotic appearance. Cultures of material from the involved nails showed Monilia albicans, as did the cultures of material from the large ulcer crater.

The peripheral arterial circulation of the lower extremities is greatly reduced.

The urine was normal. The Wassermann reaction of the blood was negative, and the sugar content was normal. A complete blood count, with differential count, was relatively normal with the exception of 2 per cent eosinophils. There has not been an opportunity as yet to have the oscillometric findings recorded. The blood pressure was 138 systolic and 68 diastolic.

While thromboangiitis obliterans was at first suspected, further examination classified the condition as obliterative endarteritis. It is a question whether the involvement of the nails is primary or secondary to the peripheral vascular impairment.

DISCUSSION

DR. LOUIS A. BRUNSTING, Rochester, Minn.: In this instance it would seem that the infection of the nails by Monilia is a secondary incident to the primary disease, which is thromboangiitis obliterans with incipient gangrene of the distal phalanges.

DR. F. W. LYNCH, St. Paul: In a recent article (*Am. J. M. Sc.* **202**:822, 1941) M. Naide discussed the relationship between fungous infections and thromboangiitis obliterans. The author pointed out the frequent association of mycotic infections between the toes and vascular diseases, the high incidence of positive reactions to cutaneous tests with trichophyton extracts and the frequency with which an acute exacerbation of mycotic infection preceded the onset of an attack of phlebitis. He goes so far as to suggest that the relationship may be causative rather than coincidental.

DR. THEODORE CORNBLEET: Some of the changes one notes in Raynaud's disease are present in this man, namely, the snow white appearance of the nail bed and the obliteration of the lumens. An examination with the aid of a microscope would show probably that the capillaries are damaged.

DR. CLEVELAND J. WHITE: As far as the peripheral vascular changes are concerned, the diagnosis is a toss-up between thromboangiitis obliterans and obliterative endarteritis. The recent authorities favor obliterative endarteritis rather than thromboangiitis obliterans, although the latter can occur in the fingers first. Observers at the University of Chicago considered the disease an obliterative condition. It is probably a type of endarteritis obliterans that is seen on the foot. As Dr. Brunsting brought out, the two conditions are probably coincidental. There is one practical point: With the involvement of the nails the conditions tend to heal rather slowly; so I think an ulcerative influence is brought into play. The lesions on the fingers are probably secondary.

Pityriasis Rosea with Lesions Occurring in Scars of Lupus Erythematosus. Presented by DR. HERBERT RATTNER and DR. MAURICE DORNE.

J. E., a Negro aged 15, had lupus erythematosus in 1938, which has left depigmented scars on the scalp, eyelids, face, ears, neck, chest and back. About three weeks ago an eruption developed which was typical of pityriasis rosea, with lesions on the trunk and in the scars of the lupus erythematosus on the face and neck.

Histologic examination of tissue from the neck showed a flattened epidermis with a loss of the rete pegs. The granular layer was continuous, the basal layer was intact and there was but slight edema. The upper part of the corium stained poorly and was edematous. There was a loose infiltrate in this layer composed largely of lymphocytes with fewer histiocytes and connective tissue cells. There was an extension of the infiltrate deeper about the vessels. Pigment was absent from the epidermis and corium in the center of the lesion but was present in the epidermis and in large chromatophores in the corium at the border. The Weigert stain showed no degeneration of the elastic fibers but a complete disappearance of these fibers in the upper part of the corium.

A biopsy of a specimen from the body showed changes consistent with the diagnosis of pityriasis rosea.

DISCUSSION

DR. M. R. CARO: There is no question in my mind about the diagnosis of pityriasis rosea for the eruption on the body. The lesions on the face showed no histologic evidence of lupus erythematosus. There were no changes in the elastic fibers, such as one would find in that disease. I think, however, that the facial lesions can be accepted as the end stage of lupus erythematosus.

Favus. Presented by DR. S. J. ZAKON and DR. T. BENEDEK (by invitation).

S. D., a boy aged 13, a Jewish refugee from Vienna, presents an eruption on the scalp of eleven years' duration. Examination shows the presence of scutula on two areas of the scalp, with alopecia and atrophy.

Histologic examination of the hairs and crusts showed favus. Cultures demonstrated Achorion schoenleinii. Examination with ultraviolet radiation with a Wood filter showed fluorescent hair throughout the scalp.

DISCUSSION

DR. S. J. ZAKON: This patient is from the same orphanage as the previous patient, but he happens to be a refugee. We plan to see what diethylstilbestrol will do for favus.

DR. UDO J. WILE, Ann Arbor, Mich.: Are you isolating this patient from the others?

DR. S. J. ZAKON: No, he is being given just the ordinary care. He had lived with an older boy and slept in the same bed. The other boy is free from favus.

MANHATTAN DERMATOLOGIC SOCIETY

DAVID L. SATENSTEIN, M.D., *President*

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May 12, 1942

Pemphigus Vulgaris (Chronic Benign Type) of the Nose, Lip, Mouth and Throat. Presented by DR. E. WILLIAM ABRAMOWITZ.

J. M., a married woman aged 73, was born in Germany and has been in this country for fifty-seven years. For almost forty years she has been taking bromides, valerian and later phenobarbital for various complaints. She has been wearing dental plates for the last twenty years. Her blood pressure is about 170 systolic. She had a vaginal plastic operation several years ago and now is wearing a pessary. Her menopause appeared twenty years ago. A moderate enlargement of the liver and spleen was detected about one year ago, the cause

of which has not been determined by her physician, Dr. Milton A. Miller. Her blood count shows a moderate secondary anemia.

The present eruption appeared about two years ago, starting on her tongue. It now involves the lower part of her nose, the nostrils, the upper lip and the mucous membrane of the cheeks, tongue and throat. There are no cutaneous lesions on the rest of the body. The mucous membrane presents numerous painful eroded lesions. The lower part of the nose and nostrils are red and somewhat swollen, with bleeding and crusting of the inside of the nostrils. The skin of the upper lip is reddened, edematous and painful with scattered pustular lesions. The patient has difficulty in taking food. She has lost weight, now weighing 123 pounds (55.8 Kg.). Her general condition is fairly good. There is some grooving of the nails. There is a decided alopecia of the scalp with a history of familial baldness, which is also present in one of her daughters.

All medicaments, particularly bromides, were replaced by chloral hydrate for sedation and iron for her anemia. She was given a soft diet with plenty of noniodized salt. She is receiving 100,000 U. S. P. units of vitamin A and 150,000 U. S. P. units of vitamin D daily, local application of triple dyes (gentian violet 1 per cent, brilliant green 1 per cent and acriflavine base 0.1 per cent in aqueous solution) to the affected areas and an epinephrine ointment for the nostrils. She is also using a vitamin A and D ointment with 5 per cent ethylaminobenzoate on the nose and upper lip.

The patient has been under observation about four weeks, during which time she has shown decided improvement.

No bromides were detected in a twenty-four hour specimen of urine.

NOTE.—This patient died suddenly on Sept. 26, 1942, apparently of a heart attack.

DISCUSSION

DR. SAMUEL PECK: The label chronic benign pemphigus is being seen with increasing frequency in the literature. It seems to me that the diagnosis of pemphigus should be reserved for a condition with a grave prognosis rather than for a clinical syndrome in which the main feature is a recurrent bullous eruption.

DR. E. WILLIAM ABRAMOWITZ: Cases like this are puzzling at times, particularly if the eruption is located in only one area, such as the mouth, scalp or vaginal orifice, without other lesions on the rest of the body. The condition is neither herpes nor herpetic, because these lesions are almost constant. There is some slight improvement but the lesions are never entirely gone. The general condition of these patients is good. I had to exclude bromoderma in 1 case because the patient was taking bromides for twenty years on and off. The laboratory report of a twenty-four hour specimen of urine showed bromides to be absent. I have been treating patients with pemphigus with the local application of triple dyes, large doses of vitamin A and D and a high calory mixed soft diet. In most instances there was some improvement.

Pemphigus Vulgaris (Chronic Benign Type) of the Mouth, Throat and Vaginal Orifice. Presented by DR. E. WILLIAM ABRAMOWITZ.

I. C., a married woman aged 52 years, was born in Russia and has been in this country for thirty-seven years. A uterine fibroid was removed fourteen years ago; otherwise her past history is irrelevant. Her present condition dates back to three years ago, when she began to complain of a dry throat. About two years ago blisters appeared in her throat, tongue and vagina. She was seen in February 1941 by Dr. Howard Fox, who entertained the diagnosis of a possible pemphigus. The reaction to a phytopharmacologic test was said to be positive.

The patient was referred to me in October 1941, when she showed a vesicle on the tip of the tongue and several lesions in other parts of her mouth and also in the nose. A small lesion was present at the vaginal outlet. She complained of a painful throat and dyspareunia.

She was under the care of her family physician, Dr. C. J. Scovner, and also Dr. F. E. Stone, an otolaryngologist. She received some injections of arsenic,

but they were discontinued because of a dermatitis that developed. She also received nicotinic acid and riboflavin.

She was given 100,000 U. S. P. units of vitamin A and 150,000 U. S. P. units daily of vitamin D, with triple dyes (gentian violet 1 per cent, brilliant green 1 per cent and acriflavine base 0.1 per cent in aqueous solution) applied locally and also some anesthetic lozenges. She was seen again in December 1941, when she had improved considerably.

She now presents a dime-sized erosion on the uvula with a healing lesion on the left buccal mucosa. She has no vaginal lesions now. The skin has never been involved. Her general condition has remained good.

DISCUSSION

DR. FRED WISE: It would be of great interest to keep patients with lesions of this kind under observation for long periods. It would enable one to determine the clinical changes in the eruptions as they progress, possibly terminating in one of the varieties of true pemphigus or undergoing complete regression.

DR. PAUL E. BECHET: The use of the word benign in connection with true pemphigus is misleading. Pemphigus may appear to run a slow course for one or more years, but almost invariably at varied periods it undergoes a rapid increase in bullae, with a fatal termination. I have in mind 3 private patients with a few bullae limited to the buccal mucosa for from one to three years. Their general health was excellent. After the appearance of generalized pemphigus they became ill and death occurred within six or eight months.

DR. E. WILLIAM ABRAMOWITZ: I had under treatment an old woman who had essential shrinking of the conjunctiva with an occasional lesion on the vulva. She had it for over ten years, and there were no lesions on the body.

Vitiligo of the Eyelids and Canities of the Cilia in a Child. Presented by DR. MAURICE J. COSTELLO.

A girl aged 2 years and 9 months has had vitiligo of the eyelids and depigmentation of the cilia since January 1942, which the mother claims followed a cold. The child's father has a number of vitiliginous patches on the body. There is also depigmentation of the outer edges of the eyebrows. In the past few days there has been graying of hairs in the left temporofrontal region.

DISCUSSION

DR. PAUL E. BECHET: One of the most common manifestations of vitiligo in hairy regions is the appearance of white hair over the affected areas. I prefer to confine the word canities to premature or senile grayness of the hair of a general distribution and not to use the term in describing white hairs over vitiliginous areas.

DR. HOWARD FOX: The proper term for gray hair, whether it is the hair of the scalp or the eyelashes, is canities.

DR. MAURICE J. COSTELLO: The father of this child has a number of vitiliginous patches on the body and extremities. I should like an expression of opinion of the members with regard to the advisability of administering paraaminobenzoic acid to this patient since the condition is of such recent origin.

NOTE.—The patient has been taking a 100 mg. tablet of paraaminobenzoic acid daily for the past two months since she was presented in May. The condition has been definitely improved, and no untoward reaction has been observed.

DR. WILBERT SACHS: In the *Archives of Ophthalmology* (**27**:342 [Feb.] 1942) Zentmayer described a case of vitiligo about the eyes associated with severe uveititis, alopecia, poliosis and deafness. I wonder if this patient's eyes were examined?

DR. E. WILLIAM ABRAMOWITZ: An editorial in *The Journal of the American Medical Association* (**118**:302 [Jan. 24] 1942) stated that the evidence on behalf

of some definite relationship between the intake of vitamins and the graying of hair is far more convincing for panthothenic acid than for paraaminobenzoic acid. If anybody should be taking paraaminobenzoic acid and the need for sulfonamide compound arises, the acid will nullify the action of the sulfonamide drug.

DR. JACK WOLF: I have been treating patients with vitiligo with paraaminobenzoic acid for about two months and have not seen anything happen except the development of new areas of vitiligo in some patients.

DR. SAMUEL PECK: I have had a rather limited experience with the use of paraaminobenzoic acid in cases of vitiligo and canities. The longest period of observation in any case has been eight months. The maximum dose administered has been 300 mg. per day. To date I have seen no effect as far as the return of the black color of the hair is concerned.

Dermatitis Herpetiformis in a Child. Presented by DR. MAX SCHEER.

F. T., a boy aged 9 years, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 28, 1942, at which time he presented cutaneous lesions of two years' duration. The onset followed measles and scarlet fever. He "broke out with blebs and eruptions on the scalp, body and arms." He was hospitalized and the lesions cleared entirely with sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) therapy, but they recurred when he went home.

The face, anterior surface of the neck, upper part of the chest, axillas, groins, forearms and legs are involved. The eruption consists of edematous red to reddish blue papules, with numerous pinhead-sized to pea-sized bullae, many of which are ruptured and covered with yellow crusts. The bullae are thin walled but fairly tense. In certain areas, principally on the forearms and legs and under the axillary folds, the tendency is toward confluence, while in other areas, as on the scalp, the bullae are more or less discrete. There is no scaling or atrophy. On the back, which is at present relatively free of the lesions, a few pigmented macules are present.

The hemogram was normal except for 10 per cent polymorphonuclear eosinophils and 11 per cent band neutrophils. The patient is being treated now with 5 per cent sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) ointment and starch baths.

DISCUSSION

DR. GEORGE LEWIS: This patient presents a beautiful example of a pruritic bullous eruption in a child. I think the characteristics of dermatitis herpetiformis are present.

DR. FRED WISE: The improvement in this patient's eruption was due to the application of a 10 per cent ointment of sulfathiazole. The drug was not administered internally as the child lives out of town and medication could not be controlled. In my opinion, administration of an arsenical compound in sufficiently large doses is an excellent remedy for dermatitis herpetiformis in most cases.

DR. E. WILLIAM ABRAMOWITZ: It has been my experience that the eruption is affected favorably by sulfonamide compounds but recurs when administration of the drug is discontinued. Roussel of New Orleans recommended chromium sulfate in doses of 0.25 Gm. in capsules three times daily and less for children (ARCH. DERMAT. & SYPH. **30**:128 [July] 1934). I gave this treatment to a little boy with dermatitis herpetiformis, and the condition responded to this medication, but I do not know whether it recurred or not.

DR. ISADORE ROSEN: I agree with the diagnosis as presented. The problem in this case is one of therapy. The boy should be placed in a hospital, where he could receive warm potassium permanganate baths (1:8,000) for periods of three or four hours at a time. Along with this I should suggest arsenic in some form of dosis tolerata.

DR. ANTHONY C. CIPOLLARO: The history revealed that this boy improved under treatment with sulfapyridine while he was in the hospital. I see no reason why administration of the drug in small doses should not be continued as long as the patient tolerates it and as long as the condition remains under control.

DR. SAMUEL PECK: My enthusiasm for the use of sulfanilamide and its derivatives in the treatment of dermatitis herpetiformis has rapidly vanished. This is due to the fact that, although after the administration of full dosage a brilliant result is obtained, there is a recurrence when use of the drug is stopped. Small maintenance doses are inadequate to prevent recurrences, and I do not think it either advisable or safe to continue large doses of these drugs over long periods.

DR. GEORGE LEWIS: Sulfathiazole ointment worked well in 1 patient. He experienced relief from the itching, and there was some improvement in the eruption. He has not had a relapse for one month.

DR. DAVID BLOOM: It is my impression that not enough caution is exercised in administering the sulfonamide drugs. Sensitization to the drug should be kept in mind. If a patient does not respond to a course of any of these drugs this treatment should not be repeated.

DR. ANTHONY C. CIPOLLARO: Perhaps I did not make myself clear: I said that I think sulfonamide compounds should be used as long as the patient tolerates them and as long as the patient continues to improve under this treatment.

DR. MAURICE J. COSTELLO: I agree with Dr. Peck that the maintenance dose is larger than the safe dose for patients suffering with this disease. I think it is dangerous to administer such a drug over long periods in therapeutic amounts.

DR. MAX SCHEER: The little experience I have had with sulfonamide compounds in the treatment of dermatitis herpetiformis has been with sulfathiazole. I have found that as soon as the use of sulfathiazole is stopped a recurrence takes place within a few days or a week. I followed up 1 patient at the Mount Sinai Clinic. The patient had a constant series of recurrences, and for that reason I do not think it is safe to give sulfathiazole or any of the sulfonamide drugs to such patients. Drs. Rosen and Wise spoke favorably of the administration of arsenic and even giving it in big doses. To that I am opposed, because I have never seen a permanent cure from it. There will come a time when some of the patients will have arsenical keratoses and epitheliomas.

Granuloma Annulare. Presented by DR. MAX SCHEER.

A. Y., a girl aged 4 years, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Feb. 28, 1942, at which time she presented an eruption of fifteen months' duration. The family history and the past history were irrelevant. The child has not had the usual diseases of childhood. She is several pounds overweight and has been in good health except for frequent colds during the past year.

The present illness began in the left popliteal region with a raised patch 3 inches (7.5 cm.) in diameter. This was treated with a 10 per cent ammoniated mercury preparation, which caused a dermatitis and resulted in a "cure." A year ago a new patch developed, on the right hand; two weeks later a patch developed on the left ankle, and three months after that a patch appeared on the right sole. These lesions never regressed.

At present there are four lesions. They are painless, nontender and nonscaly. On the hand the patch measures 2 by 2.5 cm. and is uniform, oval, dull purplish red, level with the surrounding skin and not infiltrated. On the outer side of the left ankle the patch is 7 by 5 cm. and has a slightly raised and infiltrated border about 2 mm. in width. On the right sole are two plaques. One is anterior to the heel and measures 1 by 2 cm. The other is 2 by 2.5 cm. and is at the head of the first metatarsal. These two lesions are irregular, rounded,

solid, raised, yellowish brown and somewhat infiltrated. All the lesions fade on diascopic pressure, leaving a faint uniform yellowish zone.

The hemogram was normal except for a diminished red blood cell count, of 3,770,000. Intracutaneous tuberculin tests with concentrations as low as 1:10,000 elicited negative reactions. A roentgenogram of the chest was normal.

The patient received 75 r of unfiltered roentgen rays to all the lesions once weekly (total 600 r), with some improvement.

A section taken from the left foot was examined by Dr. Charles F. Sims and diagnosed as granuloma annulare.

Lymphangioma. Presented by DR. JACK WOLF.

E. L., a man aged 22, is presented with the diagnosis of lymphangioma. His history is peculiar in that he states that for the past eight years, possibly longer, the eruption has recurred several times during the course of the year and has completely healed between attacks.

When first examined, on March 17, 1942, he presented an eruption consisting of closely grouped hemorrhagic vesicles which extended in bandlike zosteriform fashion from the midline to the left anterior axillary line along the lower portion of the abdomen. The vesicles were tense. Some were already dry and gave the impression of being ready to fall off, leaving a clean, healthy-looking surface. The diagnoses of herpes simplex recurrens (hemorrhagic) and hemolymphangioma were considered at that time.

The patient was not seen again until this evening. The clinical picture has altered considerably. The eruption is hemorrhagic in spots, and other vesicles are filled with a clear fluid. The entire affected area is elevated to about one-third to one-half the extent it was previously.

DISCUSSION

DR. JACK WOLF: When Dr. Wise and I saw this patient originally the picture was not quite like what it is tonight. The entire area was hemorrhagic. The interesting thing is that this man says the eruption clears up completely.

Lupus Erythematosus Associated with Idiopathic Infantilism in a Child. Presented by DR. ISADORE ROSEN.

G. S., a boy aged 10 years, has had an eruption on the face since the age of 2 years. It consists of erythematous telangiectatic plaques on the bridge of the nose and adjacent parts of the cheeks. There is hardly any scaling, and only mild atrophy is present.

On the trunk there are numerous café au lait spots. In the coccygeal region there is an indentation suggesting a pilonidal cyst.

The boy is much smaller in stature than normal for his age. The expression of his face has a senile quality, but his voice and his general behavior are typical of a young child. In the pediatric department of the New York Post-Graduate Medical School and Hospital, where he was studied, a diagnosis was made of idiopathic infantilism of the Lorain type.

Wassermann and Kahn reactions of the blood were negative, and the spinal fluid was normal. The blood count was normal, but the basal metabolic rate was 9 per cent below normal. A roentgenogram of the skull revealed "bony structures small for his age but otherwise normal." Epiphysial development of the long bones was compatible with his sex and age. There were underdevelopment and lime salt deficiency of the bony structures of both feet.

The family history and the past history of the boy were essentially irrelevant.

DISCUSSION

DR. HOWARD FOX: If this boy has lupus erythematosus, the disease first appeared at an unusually early age.

DR. DAVID BLOOM: I believe that the vascular disturbance of the skin of the face shown by the lupus-erythematosus-like eruption is to be considered one of many malformations which the patient presents, all of which are congenital.

DR. MAURICE J. COSTELLO: I do not think this patient has lupus erythematosus. The hyperpigmented lesions may be a *forme fruste* type of Recklinghausen's disease, and this may all be part of a congenital anomaly. A biopsy would probably prove this point. I have seen such telangiectases associated with major ectodermal congenital anomalies.

DR. PAUL E. BECHET: The location of the lesions favor the diagnosis of lupus erythematosus, and their appearance suggests the telangiectatic type.

DR. FRED WISE: The eruption is not, in my opinion, lupus erythematosus, although there is a remote resemblance to it. A peculiar eruption on the cheeks, manifested by telangiectasia and superficial atrophic and pigmented spots, is sometimes encountered on the cheeks of imbecile children and children suffering from severe and chronic dyshormonal conditions often associated with microcephalus.

Basal Cell Epithelioma with Spindle Cell Changes Following Irradiation.
Presented by DR. JACK WOLF.

T. C., a man aged 52, presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, gives a history dating back to 1934. At that time a lesion on the nose clinically diagnosed as a basal cell epithelioma was destroyed with surgical diathermy. Two years later, at another hospital, a piece of tissue removed for histologic examination revealed a basal cell epithelioma. At that time he received 5 skin units (1,500 r) of unfiltered roentgen rays. He remained well until 1941, when he had a recurrence of the disease.

The histologic picture at that time was that of a basosquamous cell epithelioma rather than of a basal cell epithelioma. The patient received radon treatment, 2,548 millicurie hours with a wax mold 1 cm. thick. Some months later the basal cell epithelioma was still present at the edges, and since surgical therapy would have caused much deformity gold radon seeds were inserted at the edges of the lesion. The result was apparently good. Within two months, however, small ulcers appeared at the sites of insertion of the seeds.

Tissue removed from one of the ulcers was diagnosed as spindle cell carcinoma. The question is whether one is dealing with epithelioma or whether the histologic changes are benign and are the result of trauma from the implantation of radon.

The nose shows a considerable amount of deformity as a result of previous therapy but is well healed except for the ulceration at the edges of the lesion on the left side.

DISCUSSION

DR. WILBERT SACHS: I believe that this patient's condition should be called a continuation rather than a recurrence. It is the same lesion which has not been entirely removed. I do not believe that there is any transformation of the cells. When a basal cell epithelioma starts to infiltrate into sclerotic tissue, it is common for the cells to become spindle shaped. Spindle-shaped cells may be of any origin, but spindle cells can be only of mesenchymal origin. Therefore I see no reason for instituting a new name, especially an incorrect one.

DR. DAVID BLOOM: From my experience epithelioma in this location is less responsive to treatment than in any other location. I believe that the best treatment is excision and plastic repair.

DR. ISADORE ROSEN: Had this patient been properly treated from the start the chances are there would have been no recurrence. In cases of epitheliomas in which the entire lesion has not been removed at the initial session and in which recurrences take place they become resistant to therapy.

DR. PAUL E. BECHET: I believe that recurrence of epitheliomas after irradiation with either radium or roentgen rays alone are not uncommon and are due to

timid dosage and the omission of three important additional therapeutic measures, namely, electrocoagulation, curettage and desiccation. These three methods plus roentgenotherapy have been invariably used by myself for fifteen years with excellent results.

DR. ANTHONY C. CIPOLLARO: It is my opinion that this patient was properly handled and that the intensive irradiation was justified. He just happens to have one of those infiltrating basal cell epitheliomas that does not respond to roentgen rays. One forgets that basal cell epitheliomas are relatively resistant to radiotherapy. According to the classification of the radiosensitivity of the various tumors on the basis of type of cells, basal cell epitheliomas are down about the middle of the list. I agree with the members who advise surgical therapy. I do not agree with those who perform extensive plastic surgical operations for the treatment of ordinary basal cell epitheliomas of the nose. I think that the usual procedures employed by capable dermatologists are effective for curing lesions of this type.

DR. WILBERT SACHS: If a basal cell epithelioma is insufficiently removed a scar will form and the remaining lesion will infiltrate through this and the cells take on a spindle shape. This process may occur whether the tumor is removed surgically or destroyed by radiation. In the morphea type of basal cell epithelioma the cells may be spindle shaped without previous therapy.

DR. JACK WOLF: The condition which the patient presents brings up several problems. One is the question of adequate treatment. The best hope and the best chance of permanent cure is to treat basal cell epitheliomas adequately at the onset. However, not every basal cell epithelioma which receives what is considered adequate treatment remains well. In a certain percentage of cases recurrence takes place in spite of adequate treatment. I should like to call attention to an article by H. E. Martin and F. W. Stewart entitled "Spindle Cell Epidermoid Carcinoma" (*Am. J. Cancer* **24**:273 [June] 1935). The authors called attention to a similar pathologic picture in a number of patients previously treated and receiving roentgen ray or radium therapy. It occurs also in lesions with a great deal of sclerosis not treated with roentgen rays. They are very resistant to further irradiation. They do not do well with any treatment except wide excision.

Tuberculosis Cutis of the Nose. Presented by DR. PAUL E. BECHET.

A. C., a woman aged 53, presented from the New York Skin and Cancer Hospital, states that the lesions on the nose began six years previously. The family history is irrelevant except that her husband died of tuberculosis. The patient has active pulmonary tuberculosis.

On examination one discerns on both alae of the nose fairly well defined infiltrated areas with several various-sized ulcerations covered with thick brown crusts. The right ala is partially destroyed. Some of the ulcerations have coalesced to form a semicircular configuration.

Roentgenograms of the chest showed an extensive tuberculous involvement of the upper lobes of both lungs. Intracutaneous injections of old tuberculin gave a plus-minus reaction to a dilution of 1:1,000,000, a 2 plus reaction to 1:100,000 and a 3 plus reaction to 1:10,000. Examination of the nasal discharge was negative for acid-fast bacilli. Repeated serologic examinations of the blood for syphilis gave negative results. However, on April 23, 1938 a histologic diagnosis of syphilis was made.

Twenty intramuscular injections of bismuth subsalicylate and eight intravenous injections of neoarsphenamine had no therapeutic effect.

DISCUSSION

DR. WILBERT SACHS: The tissue was not taken deep enough. All that one sees is granulation tissue in the upper part of the cutis. There may be tubercles in the deeper structures. In this case the granulation tissue may be either part of the process or due to a secondary infection. There is no evidence of secondary infection in this section. I saw none of the features of syphilis.

DR. MAURICE J. COSTELLO: I think that the diagnosis of microaerophilic hemolytic streptococcic infection should be entertained in this case, because of the clinical appearance of the lesion, which is not typical of lupus vulgaris. I suggest anaerobic bacteriologic studies to determine the causative organism. I presented a woman with the diagnosis of pyogenic ulceration on the nose before this society on Feb. 8, 1938 (ARCH. DERMAT. & SYPH. **38**:106 [July] 1938). The consensus of those present was that she had some form of cutaneous tuberculosis because of a history of pulmonary tuberculosis and papulonecrotic tuberculid in childhood. Laboratory examination later revealed a microaerophilic streptococcus as the causative organism.

DR. E. WILLIAM ABRAMOWITZ: I believe this case is one of lupus vulgaris exulcerans, irrespective of the histologic observations. It is difficult for the histologist in such cases to say definitely whether the disease is tuberculosis or syphilis.

DR. GEORGE LEWIS: I am in favor of a diagnosis of tuberculosis.

DR. HOWARD FOX: I think this patient undoubtedly has tuberculosis, probably of the lupus vulgaris type. From the standpoint of terminology this should not be called orificial tuberculosis. This term usually refers to ulcers in the mouth, on the lips or in the anal region, which are secondary to pulmonary or intestinal tuberculosis respectively.

DR. PAUL E. BECHET: The patient's husband died of tuberculosis, and she has active tuberculosis, as evidenced by a physical and roentgenogram examination. Under these circumstances I believe that the correct diagnosis is tuberculosis cutis orificialis and not lupus vulgaris.

A Case for Diagnosis (Alopecia Cicatrisata? Favus?). Presented by DR. MAURICE J. COSTELLO.

J. G., a boy aged 9 years presented from the Bellevue Hospital, has a quarter-sized oval area of cicatrizing alopecia in the left parietal region which has been present since he was 1 year old. In addition, there is a small scaly erythematous lesion in the parieto-occipital region.

Scrapings from these lesions this afternoon were normal, but from similar lesions on July 17, 1941 Achorion schoenleinii was found on culture. At that time the patient's younger sister had similar lesions on the scalp. Fungi were also found in these lesions. Both were treated by epilation with roentgen rays in August and September 1941.

DISCUSSION

DR. GEORGE LEWIS: The diagnosis of favus has been established, and I believe the alopecia that is present now could have been caused by the previous active favus. I should be against making a second diagnosis. There are probably still some active lesions. It is not always easy to find the organism in isolated foci, but repeated search in marginal hairs might be fruitful. Alopecia cicatrisata is rare in children and need not be considered in this case.

DR. PAUL E. BECHET: The age of the patient and the localization are against the diagnosis of folliculitis decalvans.

DR. MIHRAN B. PAROUNAGIAN: I have observed a great many cases of favus, and it seems to me that after nine years there should be only atrophy and no active lesions such as this patient presents. I am not able to account for the follicular eruption.

DR. ANTHONY C. CIPOLLARO: The best single treatment for favus and other forms of fungous infections of the scalp is administration of an epilating dose of roentgen rays.

DR. HOWARD FOX: This was a proved case of favus a year ago, and in my opinion favus is still active. No one has mentioned the presence of tiny pustules about which Sabouraud often wrote. In answer to the statement that after a certain number of years the activity of favus always ceases, it is only necessary to mention the case recorded by Sabouraud of a man aged 80 with active favus.

A Case for Diagnosis (Dermatitis Due to Sulfathiazole?). Presented by DR. ISADORE ROSEN.

M. R., a white woman aged 31, came to the New York Skin and Cancer Hospital on May 4, 1942 with an eruption of one week's duration which started on the dorsa of the hands and spread to all parts of the skin within a few days.

The eruption, which is now of nineteen days' duration, involves the whole body except the palms and soles. It is most pronounced on the upper part of the chest, on the forearms and under the breasts. It consists of round, lentil-sized, erythematous, flat, hardly raised lesions which show a scaly collaret at the periphery. In some areas the lesions coalesce to form irregular plaques. In the groins there is a sharply defined plaque with raised borders. The webs of the toes show erythema and scaling. The nose and the adjacent parts of the cheeks show diffuse erythema and slight scaling. The scalp shows considerable scaling. The eruption is associated with moderate pruritus.

The patient states that she received sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) medication for a sore throat from April 15 to April 17, ten days before the eruption appeared.

The Wassermann reaction of the blood was negative, and the blood cell count and differential leukocyte count were essentially normal. A mycologic examination of the feet and toes gave negative results microscopically.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: I saw this patient at the clinic. In my opinion she has a generalized psoriasis.

DR. DAVID BLOOM: Since the eruption looks unusual for psoriasis or seborrheic dermatitis and since there is a definite history of the ingestion of sulfathiazole, this drug has to be suspected to be the causative agent of the eruption.

DR. SAMUEL PECK: While the clinical appearance of the eruption suggests psoriasis, I should be willing to make a diagnosis of pityriasis rosea.

DR. MAURICE J. COSTELLO: In studying cases at Bellevue Hospital I have noticed seven types of toxic cutaneous manifestations following the administration of sulfathiazole. From the clinical appearance I think that this patient has psoriasis rather than a dermatitis following the administration of one of the sulfonamide compounds. In 1 of the patients erythema nodosum developed after treatment with sulfathiazole and recurred when sulfadiazine (2-[paraaminobenzenesulfonamido]-pyrimidine) was substituted for it.

DR. MIHRAN B. PAROUNAGIAN: I noticed some lesions on the lower extremities which were suggestive of psoriasis.

DR. GEORGE LEWIS: There seem to be at least three distinct types of lesions. The majority of the lesions resemble psoriasis. There is a well defined tinea-like eruption in the groin, and a solitary lesion is present which could be ringworm or pityriasis rosea. The third variety of eruption can be noted on the anterior surfaces of the wrists, where there are a number of violaceous, shiny, flat-topped papules which are suggestive of lichen planus. Since there are cases of lichen planus beginning with lesions simulating pityriasis rosea, I should like to suggest a diagnosis of lichen planus, the typical eruption of which will appear later.

DR. PAUL E. BECHET: In my opinion the woman has a guttate psoriasis and the sulfathiazole is not responsible for the eruption.

DR. MAX SCHEER: I think this patient has acute psoriasis of the guttate type. I scraped some of the guttate lesions and got silvery scales.

DR. HOWARD FOX: I think the evidence in this case is against an eruption due to one of the sulfonamide compounds. As Dr. Costello brought out, none of these drugs had been administered before the eruption appeared. One of these drugs might, of course, produce a psoriasis-like eruption, just as arsenic can cause an eruption that is indistinguishable from lichen planus.

A Case for Diagnosis (Lichen Scrofulosorum?). Presented by DR. DAVID BLOOM.

J. L., a Negro aged 9 years, was previously presented before the Bronx Dermatological Society in April 1942 (ARCH. DERMAT. & SYPH. **46**:939 [Dec.] 1942).

DISCUSSION

DR. HOWARD FOX: The patches of grouped follicular papules look strikingly like lichen scrofulosorum. In most cases of this disease, however, the eruption is associated with active pulmonary tuberculosis. Incidentally, I have never been able to learn why lichen scrofulosorum is such a rarity in the United States.

DR. WILBERT SACHS: The slide I saw showed no evidence of lichen scrofulosorum.

DR. DAVID BLOOM: Although the eruption looks clinically like lichen scrofulosorum, a similar picture is seen in Nékám, L.: Corpus Iconum Morborum Cutaneorum, Leipzig, Johann Ambrosius Bart, 1938, vol. 5, pts. 1-3, illustration 993. There are a number of points which do not permit such a definite diagnosis. First, there is no reaction to tuberculin in any concentration, while lichen scrofulosorum is usually associated with hypersensitivity. Secondly, there is no tubercle formation present on microscopic examination of the tissue. Another biopsy, however, will be made and serial sections examined, which may perhaps reveal a specific structure and thus establish the diagnosis.

Xanthoma Tuberosum and Tendon Xanthoma. Presented by DR. FRED WISE.

The patient was presented before the New York Dermatological Society on April 21, 1942 (Case for Diagnosis [Xanthoma Tuberosum and Tendon Xanthoma?], ARCH. DERMAT. & SYPH. **46**:929 [Dec.] 1942). His diagnosis is presented now as xanthoma tuberosum and tendon xanthoma because a histologic examination revealed groups of xanthoma cells and cholesterol crystals. The partition of the serum for lipids showed a hyperlipemia and hypercholesteremia.

DISCUSSION

DR. DAVID BLOOM: Clinically the lesions do not fit exactly into the picture of xanthoma tuberosum; the overlying skin does not show any yellowish discoloration and is not attached to the subcutaneous tumors. As I understood, the microscopic picture differs also from that of xanthoma tuberosum. It will be of great interest to follow up this case in order to place it in the correct classification.

DR. FRED WISE: The microscopic examination confirmed the diagnosis of xanthoma.

LOS ANGELES DERMATOLOGICAL SOCIETY

KENDAL FROST, M.D., *President*

ARTHUR FLETCHER HALL JR., M.D., *Secretary*

Feb. 10, 1942

Syringocystoma. Presented by DR. MAX J. WOLFF.

Mrs. V. N., a 30 year old white woman, has noticed gradually increasing numbers of lesions since the age of 14. She now shows numerous reddish yellow, pinhead-sized to match head-sized, roundish, dome-shaped or flat, soft nodules distributed symmetrically in the clavicular, suprasternal and sternal regions, with fewer lesions on the lower part of the chest, front of the neck and lower eyelids.

Histologic examination of one of the nodules showed normal epidermis with the basement membrane intact. In the corium were numerous round, oval or irregularly shaped spaces, some containing colloid material, which were lined with two or more layers of epithelium. Epithelial bands extended from some of the cysts.

DISCUSSION

DR. H. C. LINDSAY: I agree with the diagnosis.

DR. IRVING BANCROFT: What treatment is going to be pursued?

DR. M. J. WOLFF: This patient is not particularly interested in treatment. I thought the members would be interested in observing the case.

Folliculitis Decalvans (Possible Lupus Erythematosus). Presented by DR. PAUL D. FOSTER.

Miss V. A. H., a 53 year old white woman, five years ago noticed her hair coming out in spots; the alopecia cleared temporarily, and three years ago the hair returned. In October 1941 she gave a history of the disease growing increasingly worse and complained of a pulling, aching sensation in the center of the scalp (there was a little red spot in this area). She now shows many small cicatricial lesions appearing in the scalp. In the development of these lesions there were small red papules around the borders. The hemogram and the urine were normal. The reaction to serologic tests for syphilis and tuberculin tests were negative.

Eleven intramuscular injections of bismuth subsalicylate (2 grains [0.13 Gm.] each) and nine treatments with carbon dioxide slush have been administered.

Folliculitis Decalvans (Possible Lupus Erythematosus). Presented by DR. PAUL D. FOSTER.

Mrs. K. R., a 26 year old white woman, shows on her scalp multiple areas of loss of hair, with erythematous borders and scarred depressed centers, ranging in size from a few millimeters to 2 cm. in diameter. The first lesions appeared about three years ago and, according to the patient, are essentially the same in appearance now as they were twenty-five or thirty months ago.

The hemogram and the urine were normal; the values for nonprotein nitrogen, sugar and total protein content of the blood were normal. Roentgen examination of the teeth and sinuses showed no foci of infection. Treatment has consisted of ultraviolet irradiation, administration of vitamin A, four injections (25 mg. each) of gold sodium thiosulfate and seven injections (2 grains [0.12 Gm.] each) of bismuth subsalicylate.

DISCUSSION OF TWO CASES OF FOLICULITIS DECALVANS

DR. SAMUEL AYRES JR.: I should like to bring up the differentiation between folliculitis decalvans and pseudopelade of Brocq. I am not sure that I have ever encountered a case of folliculitis decalvans; the pseudopelade of Brocq as I understand it is more of a slowly spreading, almost cicatrizing process in which the follicles almost disappear. I suggest a diagnosis of pseudopelade.

DR. CHRIS HALLORAN: I thought the same as Dr. Ayres in these cases.

DR. H. C. L. LINDSAY: Pseudopelade appears like misplaced lichen sclerosus in the scalp. The lesions in the cases presented do not appear like pseudopelade but strongly simulate folliculitis decalvans.

DR. FRANKLIN I. BALL: I do not think either diagnosis is correct. There is no regeneration of hair in either disease. One of the patients had hair grow back which did not fall out again.

DR. JULIUS SCHOLTZ: I was not convinced that there was any scarring. If hair follicles remain in the skin, the diagnosis of alopecia areata might be considered. The patient states that hair has regrown where the specimen for biopsy was taken. If roentgen treatment will regrow hair (as has been reported in the

literature), in my opinion removal of tissue for biopsy should be equally efficacious treatment.

DR. KENDAL FROST: There is a clear differentiation between folliculitis decalvans and pseudopelade. I should call the disease in both of these cases folliculitis decalvans.

DR. H. C. L. LINDSAY: There is definite atrophy. Usually the local treatment of alopecia areata is a counterirritant. This makes the area red as if inflammation were present and due to the disease, whereas it may not be. The patient has had this disease a long time. Any anticipated recurrence and spread of the disease should have been in evidence by now.

DR. PAUL D. FOSTER: I do not know what the diagnosis is either. When I first saw the lesions they were all the size of a pea and had been present a long time. Some of the areas were erythematous, and I took specimens for biopsy from those areas. I lean toward a diagnosis of folliculitis decalvans, but not too far that way. Using solid carbon dioxide with acetone I touched each lesion with an applicator, not enough to cause a reaction.

Xerosis of the Skin Treated with Concentrated Vitamin A. Presented by DR. FRANKLIN I. BALL.

R. V., an 11 year old white boy, has had since birth a brownish scaly hyperkeratotic eruption on the arms and legs. It is always worse during the winter but tends to clear up during the summer, when he gets plenty of sunlight. The eruption affects the arms and legs especially and the abdomen. Treatment has consisted of concentrated vitamin A, two capsules (25,000 U. S. P. units each) a day.

DISCUSSION

DR. SAMUEL AYRES JR.: This patient would probably qualify as one that would benefit by vitamin A; he probably has a type of ichthyosis. I should like to see him again after two or three months of vitamin A therapy.

DR. FRANKLIN I. BALL: I think that this patient being presented now does not give a clear picture of what the condition was. Three months ago it was worse, while now there is considerable improvement. He has been under vitamin A treatment for about three months, taking 50,000 U. S. P. units daily. The child has always been better in the summer, there being no evidence of xeroderma at all. There is so much improvement it is hard to get a true picture of how the disease appeared originally. Loathe as I am to give vitamins credit, I present a case in which the condition responded to vitamins alone.

DR. WILLIAM GOECKERMAN: Undoubtedly a physiologic or biochemical response is not uncommonly seen as the result of large doses of vitamin A, and I should attribute the improvement in this patient to its administration. In my opinion this does not mean that there was a vitamin A deficiency or disturbance. Vitamin A has some definite influence on the skin, possibly the nutrition, when there is no question of deficiency, but I cannot explain the mechanism.

Pityriasis-Rosea-Like Dermatitis Medicamentosa (Due to Mercury?). Presented by DR. M. E. OBERMAYER.

Mr. J. S., a 39 year old white man, has had syphilis for an undetermined period. While he was receiving a course of injections of mercury salicylate in oil intramuscularly, an erythematosquamous eruption appeared on the legs which soon spread to the groin, trunk and axillas. Antisyphilitic treatment was discontinued. As the lesions on the trunk assumed more and more the aspect of those of pityriasis rosea, the therapy was again instituted, this time in the form of intramuscular injections of bismuth subsalicylate in oil. The eruption continued to develop for a while and

then cleared to the present level while the treatment was continued. Previous therapy, including neoarsphenamine, mercury and bismuth, was well tolerated.

He now shows oval macules, which measure from 1 to 2 or 3 cm. in diameter, arranged with their long axes along the lines of cleavage, scattered over the trunk and thighs; many of them are merely hyperpigmented, while others still show mild erythema and fine scaling. More diffuse changes of an erythematosquamous nature are present on the legs. The scalp shows diffuse scaling.

The blood count is normal, and scales macerated in potassium hydroxide showed no fungi. Histologic examination of a lesion on the right thigh showed a chronic inflammatory process of internal origin. The stratum corneum was mildly hyperkeratotic, and there was some parakeratosis; the stratum spinosum was edematous with intercellular edema and mild spongiosis in some parts. The dermis was also edematous, and its papillary layer showed vascular dilatation and an infiltrate which consisted mainly of round cells.

DISCUSSION

DR. CHRIS HALLORAN: This is the first case of this type of eruption with treatment with mercury I have encountered. It brings to mind lichen-planus-like eruptions occurring in patients receiving arsenicals or bismuth.

DR. SAUL ROBINSON: I considered the diagnosis of lichen planus after examining the lesions on the trunk. I believe that pityriasis rosea would not show areas like those in this case. I think this condition looks like lichen planus.

DR. CLEMENT E. COUNTER: I agree with the diagnosis. It is not uncommon in large clinics.

DR. L. F. X. WILHELM: Some of the lesions suggest a lichen planus type of reaction, especially the one on the penis and those around the ankle.

DR. H. C. L. LINDSAY: Some of the lesions do not disappear no matter how much one presses them.

DR. IRVING BANCROFT: Has the patient taken arsenic at any time?

DR. KENDAL FROST: The patient had all three drugs—bismuth, arsenic and mercury—before the eruption developed. All of these drugs produce delayed reactions.

DR. JULIUS SCHOLTZ: It is interesting that we can disagree on things right before our eyes. I could not detect atrophy. I am glad to observe a case of pityriasis rosea type eruption due to heavy metal. This is the type which is well recognized as due to heavy metals. So many instances of generalized erythroderma are shown in which the eruption is allegedly due to bismuth but in which it is difficult to establish this drug definitely as the cause.

DR. CHRIS HALLORAN: When did the eruption develop in relation to the last injection? [A résumé of the treatment was read by Dr. Frost.] I should still not be too sure that the eruption was caused by mercury. Many of the French investigators who wrote about lichen-planus-like eruptions occurring in patients receiving arsenicals or bismuth advise that one continue with therapy and say that in time the lesions disappear. When sections were prepared for microscopic study, those from lesions that looked like lichen planus clinically showed a histologic picture of lichen planus.

DR. M. E. OBERMAYER: I cannot agree with Dr. Halloran's suggestion. The eruption showed no features of lichen planus clinically or microscopically. I am not certain whether atrophy is present. The dermatosis may be classified as a pityriasis-rosea-like biotropic eruption in the sense of Milian, precipitated by therapy with a heavy metal, probably mercury.

DR. CHRIS HALLORAN: All dermatologists have observed cases in which bismuth or arsenical treatment is followed by lichen planus clinically and microscopically in some cases and by only increased pigmentation in others.

Wooly-Haired Nevus of the Scalp. Presented by Dr. Nelson Paul Anderson.

M. C., a 5 year old white girl, has had the present lesion, gradually enlarging, since birth. This lesion is on the left side of the scalp and consists of an irregularly oval area in which the hair is lighter in color and closely kinked. The scalp in this area is the color of café au lait, and this color also extends down in a streak on the left side of the back of the neck.

DISCUSSION

Dr. Samuel Ayres Jr.: I do not know a great deal about the patient. She has had the lesion on the scalp since birth. It is apparently a nevus of an unusual type, showing wooly hair which is nothing like the hair on other parts of the scalp.

A Case for Diagnosis (Shamberg's Disease?). Presented by Dr. Samuel Ayres Jr.

J. B., a 23 year old white man, fell about four years ago, sustaining an abrasion on the shin. This lesion healed without difficulty, but shortly thereafter a series of lesions began to develop which have continued intermittently up to the present. All of these lesions have been on the lower part of the right leg (the left leg was amputated after an automobile accident about ten years ago). The patient states that usually a lesion develops as a bright red macular spot, beginning with a pinpoint of red and becoming flat in about two weeks. It then gradually turns brown. Some of the lesions have ulcerated. A large area on the medial aspect of the leg, which first appeared about two years ago, was ulcerated for ten weeks. Two dark spots appeared within this area early in its development and have persisted. The most recent lesion, which is now present on the front of the shin, first appeared about ten days ago, and only today has the patient noticed dark spots in its area.

The eruption is limited to the lower portion of the right leg, ankle and foot. On the medial aspect of the foot and ankle are irregular, blotchy areas of brownish pigmentation. On the anterior and medial aspect of the leg, also on the outer aspects, are about eight to ten pea-sized to dime-sized, round to irregular, brownish macules, in some of which there appears to be a definite atrophic change. The largest lesion is on the medial aspect of the leg and is irregular and about dollar sized, with a dime-sized central scar covered with slight scaling. At the upper and lower portion of this pigmented area are two pea-sized, black, slightly thickened lesions. The thickening is due to scaling. On removal of the scale from the lower lesion the black color comes off also, but the upper dark macule remains. On the shin is a bright red, elongated area in the upper part of which is a pea-sized black macule. The lesion appears to be made up of petechiae. There is also slight brownish discoloration on the tops of several toes.

Previous treatment has consisted of intravenous injections of arsenic, the last one being about a year ago. He has also had a small amount of ultraviolet irradiation.

DISCUSSION

Dr. L. F. X. Wilhelm: I thought of the possibility of a Kaposi sarcoma.

Dr. Julius Scholtz: It was my impression that this patient has dermatitis factitia. The observations do not fit any other picture that I know. However, this diagnosis should not be made before all other possibilities are ruled out. A clinical picture which remotely resembles this is that of a patient I saw at the Los Angeles General Hospital in the medical service with a diagnosis of platelet cell thrombosis. The skin showed sharply demarcated, geometrically shaped areas of necrosis, the skin and subcutaneous tissue sloughing out, in areas of dry gangrene. Although this is a rare condition, and a remote possibility, the case might be studied from that point of view. Biopsy helps to make the diagnosis.

DR. ANKER K. JENSEN: My impression was that the eruption is dermatitis factitia.

DR. KENDAL FROST: That was also my impression.

DR. SAMUEL AYRES JR.: Due to what? Has the patient deliberately produced it? This patient was seen only this afternoon. Frankly, I had never seen anything like it; I could not understand the lesions. According to the patient the lesions begin with punctate red points which persist and turn brown and in some instances ulcerate. Macules have developed in two lesions, in one in the last few days. I cannot conceive of this being dermatitis factitia. It is too disabling to the patient. Usually there is some purpose in producing a dermatitis factitia.

Blastomycosis. Presented by DR. MAX J. WOLFF.

V. N. is a 21 year old Jewess. Her disorder began on the anterolateral surface of the left leg two and one-half to three years ago. The lesion healed when she was hospitalized for one month in October 1940. It was treated with rest in bed, high caloric diet, compresses of copper sulfate, roentgen rays, iodides, vaccines given intramuscularly and ascorbic acid given intravenously. Six months later the present lesion appeared on the anteromedial surface of the same leg and has been present and increasing in size during the past nine months.

She now presents an oval area about 6 by 3 inches (15 by 7.5 cm.) on the left leg with clearing in the center and areas of induration and tumefaction with small abscesses at either end.

The Wassermann reaction of the blood was negative, and a roentgenogram of the underlying bone was normal. Animal inoculation gave negative results. Histologic examination of the previous lesion showed chronic granuloma of the skin and intracutaneous abscesses. Iodides and local medication have been given for the past three weeks without benefit.

DISCUSSION

DR. SAUL ROBINSON: I have seen this patient before and followed her case in the clinic. At that time she responded to iodides and copper soaks locally, rest in bed and a high caloric diet. The lesions cleared completely. The eruption is interesting because of its reappearance. There may be spores of blastomycosis remaining in the healed tissues. I wonder if it might not be best to excise the lesions by cautery.

DR. SAMUEL AYRES JR.: Was the organism found by direct smear?

DR. SAUL ROBINSON: Yes.

DR. CHRIS HALLORAN: I think filtered roentgen rays will give the best result. However, I have observed a few cases in which wide cautery gave perfect results.

DR. SAUL ROBINSON: A considerable amount of roentgen therapy has been given in this area.

DR. H. C. L. LINDSAY: In the first case I ever observed the eruption was cured with neoarsphenamine and roentgen therapy.

DR. WILLIAM GOECKERMAN: I think that in the early stages fairly heavy doses of roentgen rays are satisfactory treatment but not when the lesions are old. I think free cautery should be the choice in this case. In the early stages give 300 r, not a quarter skin unit, and repeat in two weeks.

DR. ANKER K. JENSEN: What would happen if ionization with copper were used in a case like this?

DR. SAUL ROBINSON: How does one account for the lesion's entirely healing and then recurring?

DR. BEN A. NEWMAN: The patient was given 1 ounce (30 cc.) of saturated solution of potassium iodide daily at the time of the first attack, and when medication was stopped the lesion recurred. I do not think this is so unusual.

DR. M. J. WOLFF: The patient has had considerable roentgen treatment, and there are pigmentation and atrophy of the skin in the area. I have been reluctant to give more roentgen ray treatment.

Keratosis Follicularis (Darier) Treated with Vitamin A. Presented by DR. BEN A. NEWMAN.

J. P., a 19 year old white girl, had an itching red eruption on the neck which developed six years ago after an intense sunburn. This eruption persisted for many months and finally disappeared, leaving a mild roughness of the skin. Two years later, after the patient came to California, a similar red itching eruption developed on the neck and upper part of the chest, which was believed to be an actinic dermatitis. This eruption persisted for six months or more, and with the involution of the acute dermatitis the involved areas remained rough in appearance. About one month ago a similar itching red eruption appeared on the left side of the chest. There is no history of night blindness.

The patient presents a grayish pinhead-sized papular eruption on the sides of the neck, extending to the clavicular areas. At first glance this resembles a verrucous and papillomatous eruption; however, on closer inspection the eruption seems to be composed of groups of individual spherical and flat grayish or brown papules with minute central crusts. On the left side of the chest is a large plaque consisting of grouped pinhead-sized maculopapular lesions. There are scattered discrete crusted lesions on the shoulders and upper part of the back in which the crusts are easily removed, leaving shallow depressions. The palms present some scattered discrete keratotic papules, and there is a generalized keratosis pilaris of the extremities.

Histologic examination of a specimen removed from the shoulder exhibited typical hyperkeratosis with follicular plugs, irregular acanthosis with elongation of the rete pegs, lacunas in the lower portions of the rete, Darier cells scattered through the epidermis and a mild inflammatory reaction of the cutis, with round cell infiltration in the papillary and subpapillary layers. The patient has been taking 150,000 U. S. P. units of vitamin A daily for the past week, and a noticeable flattening of the lesions has already taken place.

DISCUSSION

DR. BEN A. NEWMAN: In a matter of five or six days of vitamin A therapy there is improvement already. Because of the inflammatory condition which ushers in this disease, which closely resembles actinic dermatitis, the patient was treated as having actinic dermatitis, and this verrucous eruption followed.

KENDAL FROST, M.D., *President*

ARTHUR FLETCHER HALL JR., M.D., *Secretary*

March 10, 1942

Callosities, Multiple, Congenital. Presented by DR. HARRY P. JACOBSON and DR. NELSON PAUL ANDERSON.

R. F., a 16 year old white boy, and his mother present similar eruptions dating from early childhood. There is roughly symmetric involvement of the plantar and lateral aspects of the feet, the lesions being made up of variously sized and shaped, light amber-colored calluses associated with a degree of tenderness here and there. There is also a fairly diffuse digital and pedal tinea.

DISCUSSION

DR. CHRIS HALLORAN: I think the patient has keratosis palmaris et plantaris.

DR. SAMUEL AYRES JR.: I agree with the diagnosis. I think there is a fungous infection, especially in the boy. There is maceration between his toes. I had a child who had the same sort of lesions complicated with a fungous infection. I think the disease is essentially hereditary.

DR. ANKER K. JENSEN: I wonder what androgenic therapy would do? A similar case has been reported, in which the condition cleared with such therapy.

DR. H. C. L. LINDSAY: In regard to androgen: Today I learned of a patient who was apparently cured of senile keratoses by administration of androgen. It would be interesting to try such treatment on this patient.

DR. NELSON PAUL ANDERSON: I do not believe that this patient has ordinary palmar and plantar keratoderma. This disease is usually diffuse. The patient presents localized areas of hyperkeratosis. He has no changes in the finger nails, though the mother has had such changes about ten years. I should be more inclined to consider pachyonychia congenita as a diagnosis. There have been several patients with this disease reported on in this country. They often have leukoplakia involving the mouth and tongue. Neither the boy nor his mother shows that. The boy has a secondary fungous infection. I do not believe that this disease belongs to the ordinary diffuse plantar keratoses, which are usually accompanied by palmar keratoses.

Juvenile Xanthomatosis or Nevoxanthoendothelioma. Presented by DR. BEN A. NEWMAN.

S. H. is a 2 year old white girl. Her mother states that she first noticed three yellow spots on the baby's scalp when she was 6 months old; during the past year and a half new spots have been appearing on the chest and extremities.

The patient now presents on the scalp three flat infiltrated yellow spots varying in size from that of a pea to that of a small finger nail. There are about eight scattered pinhead-sized to pea-sized elevated yellow papules on the chest and arms. The liver is enlarged to 1 fingerbreadth below the costal margin. Treatment has consisted of a low fat diet since the age of 6 months.

The blood and urine have always been normal. The total cholesterol content of the blood was 220 mg. per hundred cubic centimeters.

DISCUSSION

DR. M. J. WOLFF: I agree with the diagnosis of juvenile xanthoma. It is interesting to note that the cholesterol content is within normal limits in this case. A fat-free diet apparently had no effect on the lesions.

DR. C. R. ANDERSON: Hamilton Montgomery has pointed out that juvenile xanthomas are ordinary xanthomas. Nevoxanthoendotheliomas, on the other hand, spontaneously heal and disappear as time goes on. In the section I found some foreign body giant cells. Their presence in the histologic picture of nevoxanthoendothelioma has been pointed out by Montgomery. I believe that this child has this disease and not juvenile xanthomatosis.

A Case for Diagnosis (Radiodermatitis?). Presented by DR. L. F. X. WILHELM and DR. WILLIAM H. GOECKERMAN.

Miss M. Y., a 17 year old white girl, states that in May 1941 she consulted a chiropractor, who prescribed colonic irrigation, liquid diet, sitz baths and diathermy every day for the treatment of pylorospasm. After about three weeks she noticed a red lesion over her sacrum. This gradually increased in size, and after nine weeks she stopped all treatment. Since then the area has been treated with infra-red radiation, radiation from a carbon arc lamp and ointments by another physician. She now presents a lesion about 3 by 5 inches (7.5 by 13 cm.) over the sacrum; it is erythematous and infiltrated, with telangiectasia and small ulcers.

DISCUSSION

DR. NELSON PAUL ANDERSON: I think the girl has a radiodermatitis. I cannot conceive of any burn of any form other than a roentgen ray burn producing this picture. When such a lesion involves the back and lower region of the back one must suspect that the patient has had a lot of fluoroscopy. The present lesion came on about three weeks after the fluoroscopic examination. I cannot conceive of its being a lesion produced by diathermy or any other electric agent except roentgen rays.

DR. L. F. X. WILHELM: The patient said she had had roentgen ray studies by a chiropractor.

DR. H. SUTHERLAND CAMPBELL: I went into that in the history, and she stated that in her roentgen examinations the rays were directed only toward the abdomen and not toward the back. I do not think the history very dependable in this case, and I agree most definitely with the diagnosis of roentgen ray burn.

DR. ARTHUR FLETCHER HALL JR.: I agree with the diagnosis of radiodermatitis; there are well defined limiting borders as if it had been shielded to a certain area. It must have been from roentgen therapy, however, and that might be part of the history that has not come out. I can conceive that a chiropractor or some one else might try to bring about an abortion with roentgen rays; if that is what occurred in this case the history might be withheld, especially from the patient's mother.

DR. WALTER F. SCHWARTZ: I heard about this patient in Pasadena. I cannot conceive of any thermal burn's coming on three weeks after treatment. At first glance one would think of a roentgen ray burn, but a chiropractor gave the treatment and one does not ordinarily think of chiropractors' using roentgen rays. However, I know a dentist who was treated with roentgen rays by a chiropractor. I believe this patient has a roentgen ray burn because of the definite localized lesion. Scleroderma was the only disease entity that entered my mind.

A Case for Diagnosis (Vitiligo?). Presented by DR. SAMUEL AYRES JR. and DR. NELSON PAUL ANDERSON.

Mrs. L. G., a 46 year old white woman, was first seen on Aug. 28, 1939, because of white spots on her face and neck which had been present about six weeks and which appeared shortly after a thyroidectomy. The patient stated that the white spots first appeared while she was on a boat trip and she thought that they were caused by mosquito bites. At the time of the first visit a number of whitish, ill defined, nonscaly macules, ranging from the size of a pea to that of a nickel, were noted. The lesions were noninfiltrated, and there was no evidence of excess pigment about the borders, as one would expect in vitiligo. There was a diffuse flushing of the face, especially the forehead, with a dry follicular roughness. In addition to this, the patient presented a typical navy bean–sized basal cell epithelioma on the side of the nose near the inner canthus of the right eye, which had been present about a year.

The epithelioma was destroyed by roentgen rays. Because of the flushing of the face, the dry follicular scaling and the presence of Demodex folliculorum in the scales, together with the fact that the patient had used soap and water very infrequently on her face, the possibility of a type of rosacea due to Demodex was considered, and Danish ointment was prescribed. This apparently improved the texture of the skin as far as the roughness was concerned but exerted no influence on the white spots.

The patient returned again in July 1941, at which time the eruption appeared to be approximately the same as at the time of the previous visit. At this time it was noted that the whitish round to oval macules were more obvious when seen at a distance and that they were particularly evident on the forehead and the V of the neck, where they stood out in sharp contrast to the erythematous background. There were also a number of whitish patches on the cheeks. The

erythematous background also presented numerous telangiectases, especially in the center of the left cheek. At this time ascorbic acid was prescribed, even though the urinary value of vitamin C was within the normal limits.

The patient returned on March 6, 1942, at which time the eruption was still present and perhaps more noticeable than previously. The patient has never taken any thyroid since her thyroidectomy. The basal metabolic rate on March 9 was —13 per cent.

DISCUSSION

DR. CHRIS HALLORAN: This case impresses me as one of progressive telangiectasia. At present I have a pregnant woman who has the same type of lesion. Becker recently reported a series of 9 cases. Three of these were of women during pregnancy.

DR. HAL E. FREEMAN: This patient's condition is a photosensitization, in lieu of any better name for it. It started on exposure to the sun and has persisted. It would respond to nicotinic acid amide, probably.

DR. CHARLES CASKEY: I suggest solid carbon dioxide as a therapeutic possibility, using a cylinder-shaped piece, a rolling motion and not much pressure. In that way there would be no demarcated reaction.

DR. SAMUEL AYRES JR.: Everybody is ignoring the white spots.

DR. SAUL ROBINSON: The patient has vitiligo. Two areas on the lower part of the neck and the lesions on the cheeks are vitiligo.

DR. WILLIAM GOECKERMAN: I think the condition is an interesting phenomenon—something definitely unusual.

DR. CHARLES CASKEY: The patient had an operation on the thyroid; so there is definitely an endocrine disturbance.

DR. SAMUEL AYRES JR.: Personally I have never encountered a case like this. I believe that the patient has something out of the ordinary. There is no evidence of hyperpigmentation at all; there is telangiectasia with indistinct white macules. She had been out on a boat in the sun just before this.

Lupus Erythematosus. Presented by DR. CLEMENT E. COUNTER.

E. K., a 47 year old white man, has had chronic bronchitis since boyhood; thirteen years ago the first cutaneous lesion appeared on the left side of the face over the zygoma. Eight months later a dermatologist gave him four ultraviolet ray treatments, and the eruption became worse and extended over the whole face. About one year after the onset he went to the University of Chicago Hospital, where he was seen by Dr. Becker and Dr. Obermayer. Three months later, on the recommendation of a neighbor, he worked in the sun with his shirt off; almost immediately his back broke out with redness, which was demonstrated before a group of physicians by Dr. Becker as an extension of lupus erythematosus due to exposure to sun. Hospitalization followed, and he subsequently received many intravenous injections of gold sodium thiosulfate and intramuscular injections of a bismuth compound and of liver extract. He now shows erythematous patches on his nose and cheeks, continuous over the sides of his neck to the back of his ears. The scalp is free, but there are lesions on the mucous membranes of the mouth, on the soles and on the dorsa of his hands. At the Veteran's Administration Facility, Los Angeles, in 1940 he was examined for foci of infection and for tuberculosis without positive findings.

DISCUSSION

DR. SAMUEL AYRES JR.: I think that is a most interesting case in view of the extent of the lesions, especially that lesion on the bottom of the foot; that is lupus erythematosus.

DR. CLEMENT E. COUNTER: This case was presented because of the lesions on the mucous membranes and the plantar lesions. These are rarely seen in lupus erythematosus. The eruption is of thirteen years' standing. Dr. Obermayer remembered him specifically because he was in an acute condition in the hospital in Chicago. The patient has a long history of chronic bronchitis, which I believe is the focus of infection causing the continuance of the disease.

A Case for Diagnosis (Early Raynaud's Disease?). Presented by DR. PAUL D. FOSTER.

M. E., a 12 year old white girl, had considerable difficulty as a small child with tonsils and adenoids; they have since been removed. She has had no other serious illnesses. The present abnormality began about six weeks ago, at which time the fingers were swollen and erythematous. The swelling subsided somewhat but after about two weeks recurred.

At present all digits are involved except the two thumbs and the ring finger of the right hand. The lesions are limited to the extensor surfaces and the distal ends; they are erythematous, mildly inflamed and not tender. The hemogram, urinalysis and determinations of blood sugar and blood cholesterol showed no abnormalities. The Kahn and Kline reactions of the blood were negative.

DISCUSSION

DR. CHRIS HALLORAN: I suggest a diagnosis of lupus pernio.

DR. SAMUEL AYRES JR.: I suggest a diagnosis of beginning acrocyanosis. I have never seen this condition begin. Usually the hands are diffusely red and sometimes livid and cold with a great deal of hyperhidrosis. This patient's hands are certainly cold. Buerger feels that in cases like this there is a thyroid deficiency.

DR. SAUL ROBINSON: I suggest that a roentgenogram be taken of the hands to see if any bony changes are associated with the cutaneous changes.

DR. KENDAL FROST: I suggest the possibility of a drug eruption.

DR. H. C. L. LINDSAY: My diagnosis of the disease is pernio.

A Case for Diagnosis (Multiform Erythema? Prurigo Mitis?). Presented by DR. KENDAL FROST.

R. I. is a 12 year old white boy. The present lesions began appearing about April or May 1941 in successive groups, beginning with a big "bump" on the lip; lesions then spread around the mouth. There have always been "water blisters." Various local applications have been used, none of which controlled the eruption, although it has seemed to improve under some of them. Most of the applications were prescribed under the diagnosis of impetigo. I saw him first on Dec. 31, 1941, at which time the lesions were scattered over the face and scalp and were definitely impetiginous crusts. On Feb. 18, 1942 he had a new attack with crusted vesicles on erythematous bases scattered over the ears, on the lips and in the mouth. This cleared rather rapidly, and a new attack appeared on March 2, 1942, which is still progressing. The present lesions began on the face, in the hair and inside the cheeks. There were clear vesicles in groups and linear streaks with little inflammatory reaction. A few days later lesions appeared on the palms and a few on the scalp. Today the lesions on the face are scattered, discrete grouped crusts and a few vesicular relics. On the palms are vesicles in various stages of evolution. Some dried crusts and fairly large blebs containing seropurulent material are present.

The blood count showed 4,850,000 erythrocytes per cubic millimeter and 8,950 leukocytes, 49 per cent of which were polymorphonuclear leukocytes, 41 per cent lymphocytes, 6 per cent large mononuclear lymphocytes and 4 per cent eosinophils. The hemoglobin content of the blood was 81 per cent.

DISCUSSION

DR. SAMUEL AYRES JR.: I thought the patient's eruption looked like erythema multiforme. The lesions had a definite vesicular appearance. It is interesting that the youngster has geographic tongue, which has been present for some time.

DR. M. J. WOLFF: I also thought of some form of an atypical erythema multiforme.

DR. SAMUEL AYRES JR.: Has sulfanilamide been used?

DR. KENDAL FROST: Sulfanilamide has been used only locally, not internally. The case was diagnosed as one of impetigo before I observed it, and, owing to lack of cooperation, it has not been studied as it should have been. A month ago the boy had a sudden outbreak; the lesions at that time looked like widespread herpes simplex. This attack cleared in a few days. The present lesions are different from any I have seen on previous observations.

NOTE.—Since this patient was presented it has become clear that the diagnosis is dermatitis herpetiformis. The boy was given arsenic by mouth, followed by rather prompt and complete healing of all the lesions. The mother discontinued giving the arsenic immediately without orders to do so, and the lesions recurred, slowly. On resumption of the administration of arsenic the improvement began again, but because of the presence of albumin in the urine, use of the drug was discontinued.

Keratosis Follicularis (Darier) After Treatment with Vitamin A. Presented by DR. BEN A. NEWMAN.

J. D., a 19 year old white girl, was presented before the society one month ago (ARCH. DERMAT. & SYPH., this issue, page 288). The patient has received the following doses of vitamin A: 150,000 U. S. P. units daily for one week, 50,000 U. S. P. units daily for one week and 25,000 U. S. P. units daily since. There has been complete involution of the eruption except for a slight brownish pigmentation on the sides of the neck.

Multiple Idiopathic Hemorrhagic Sarcoma (Kaposi) Producing Urethral Stricture. Presented by DR. BEN A. NEWMAN.

E. L., a 75 year old white man, states that in 1937 he had a small tumor of the left toe removed surgically in an eastern hospital. This was reported to be a sarcoma, and intensive radium therapy was applied. One year later several reddish and brown spots appeared on the left leg, and shortly after their appearance there was edema of the leg. During this period a stricture of the distal urethra and meatus developed which required frequent incisions and dilatation.

He was first examined by me one year ago and at that time showed essentially the same lesions but fewer. There was a dime-sized reddish brown infiltrated flat plaque on the distal portion of the glans penis extending into the meatus. There was edema of the entire left leg and foot, and there were multiple pea-sized to coin-sized brownish red and pigmented macules and papules. There were similar lesions on the dorsum and toes of the right foot. The lesions have always responded promptly to small doses of roentgen rays (150 r each), but in recent months the lesions have been more rapid in their appearance. The penile lesion has also responded promptly to irradiation. Adenopathy has never been present. Histologic examination showed the typical picture of Kaposi's sarcoma.

DISCUSSION

DR. NELSON PAUL ANDERSON: I think this case is remarkable. The urethral stricture is interesting and has been described in the literature. What happened to this man before he saw a dermatologist? He had a lesion on his little toe, and somebody took it off, said it was a sarcoma and gave him heavy roentgen

therapy. It raises the question as to how such a mistake could be avoided. The pathologist is sometimes discredited for things not of his doing. I could see by looking at the slide that the diagnosis of a melanotic nevus or melanotic sarcoma could be made, because there is not much pigment. It is unfair simply to remove the lesion and not give the pathologist any more information; he should at least know the nationality and race of the patient and where the lesion comes from. I know of an instance in which there was a granulating lesion on one toe which looked like a granuloma pyogenicum; it was sent to a pathologist in a neighboring city, and all he could make out was pyogenic granuloma. Later lesions developed in the groin. The slide was looked at again, and the lesion was recognized as a melanoma without any pigment. The clinician expects the pathologist to see everything that he does not see and more too.

DR. BEN A. NEWMAN: The lesion cannot be very malignant if it has been present for two years. Involvement of mucous membranes is not uncommon. In this case the urethral mucous membrane was involved. When the condition is advanced enough to obstruct the urethra, the patient gets a stricture. The effect of 150 r of roentgen rays lasts about three months, after which recurrence necessitates a repetition of that dose.

KENDAL FROST, M.D., *President*

ARTHUR FLETCHER HALL JR., M.D., *Secretary*

April 14, 1942

Pemphigus of the Mouth. Presented by DR. SAMUEL AYRES JR.

H. B., an 81 year old white man, has had vesicular lesions in the mouth for about two and one-half years. The patient is edentulous but has not worn false teeth for many months. Prior to coming here he had received vitamin B, 350,000,000 units; vitamins A, B, D and G, 100 tablets; nicotinic acid amide, 50 mg. daily for ten days, and sulfanilamide, 30 grains (2 Gm.) a day for ten days, with no apparent benefit. Now the patient has been hospitalized; he was given sulfanilamide in doses of 40 to 60 grains (2.6 to 4 Gm.) a day for over two weeks and then 40 grains a day for approximately three weeks more. He was also given intravenous injections of an autogenous vaccine prepared from the raw areas on the gum containing hemolytic streptococci. On one occasion monilia was found by microscopic examination of a culture, but treatment with 5 per cent aqueous solution of gentian violet, diluted compound solution of iodine U. S. P. and also Castellani's carbolfuchsin dye failed to achieve any benefit. The patient has just completed a course of eight intravenous injections of gold and sodium thiosulfate, maximum dose 40 mg., with possibly slight improvement. During the past six weeks he has also been using inunctions of testosterone propionate, 4 mg. every other day, and has felt stronger generally. He has had two intramuscular injections of liver extract, as well as "Stuart's formula" by mouth.

At present examination reveals superficial raw areas involving the gums and buccal mucosa. At times there have been noted distended straw-colored blebs up to the size of a dime. There have been no lesions on the body.

A hemogram (three months ago) was essentially normal, showing only slight hypochromic anemia and a total of 10,200 leukocytes with 5 per cent eosinophils. The urine was normal at that time.

DISCUSSION

DR. WALTER SCHWARTZ: I think this case is similar to the one that Dr. Lindsay presented a few months ago. At that time several other cases were

mentioned. In comparing the cases one needs to mention a few common denominators. Patients with this disease are always old and have complete edentia. They do not often have pemphigus vulgaris on the body. I believe this patient's age and the lack of all his teeth are two significant factors. I suggest administration of an estrogen or an androgen for a man of his age.

DR. MAX J. WOLFF: I saw a patient last week whose pemphigus began after he had several teeth extracted. I wonder if other members have encountered cases in which pemphigus has followed extraction of teeth.

DR. SAUL ROBINSON: Can this patient have an eruption due to ingestion of phenolphthalein?

DR. SAMUEL AYRES JR.: In answer to Dr. Schwartz, this patient has been given an androgen, and he told me today that he definitely felt stronger and better; the lesions have improved this last week. I do not remember specifically mentioning phenolphthalein, but I will check on it again.

A Case for Diagnosis (Scrofuloderma?). Presented by DR. SAMUEL AYRES JR.

W. A. S., a 72 year old white man, gives no history of tuberculosis and states that his present complaint is of only three years' duration. It began on his neck with formation of nodules or tumor-like masses, which after six to twelve months would break down and discharge thick pus, finally healing. Since then additional lesions have developed on the neck, on the top of the right shoulder, in the right axilla, on the scrotum and elsewhere.

The lesions are now scattered over his body, the most active areas being on the right side of the jaw and on the neck. At the angle of the jaw are two rather large pigeon egg–sized inflammatory nodules, on the under side of which is a crusted sinus. There are a number of crusted and depressed scars and sinuses on the front and sides of the neck, but those on the front and left side are relatively inactive. There are masses of subcutaneous nodules extending from the right side of the neck to the outer aspect of the right clavicle, where there is a large inflamed fluctuant area. There are masses of glands, not reddened, in the right axilla and a few smaller subcutaneous nodules on the medial and posterior aspects of the right thigh and the medial aspect of the right leg. The Kahn and Kline reactions of the blood were negative. Acid-fast stain of smear from a lesion on the neck showed no tubercle bacilli. No evidence of actinomycosis was seen in a fresh smear. The reaction to a tuberculin patch test was moderately positive after forty-eight hours.

DISCUSSION

DR. CHRIS HALLORAN: I think the patient probably has a scrofuloderma, with the positive reactions to tuberculin. I thought of sporotrichosis on account of the lesions on the leg.

DR. KENNETH STOUT (by invitation), West Los Angeles, Calif.: Have you considered a coccidioidin test? Some of the nodules that he has on his chest look like coccidioidomycosis.

DR. HERBERT LAWRENCE: I understand a search for actinomycetes was made. Perhaps it could be followed up.

DR. H. C. L. LINDSAY: The condition looked more like actinomycosis than sporotrichosis or coccidioidomycosis. The ray fungus is not always easy to find. I had a case in which the diagnosis was almost handed to me an a silver platter. The patient had an acute exacerbation, and I found the fungus on the first examination with the microscope, but before the flare-up of the disease it could not be found.

DR. SAMUEL AYRES JR.: I saw this patient for the first time four days ago. It is unusual for scrofuloderma to develop for the first time in a man of his age. The only patients with actinomycosis I have ever seen had nipple-like projections from the mouths of the sinuses. The reaction to a tuberculin test was positive; there was an exacerbation after the test and lesions have developed on his thigh. As to the question of therapy, obviously it must be conservative.

NOTE.—Inoculation of a guinea pig with pus from a lesion subsequently elicited a positive result for tuberculosis.

Lichen Planus, Progressing in Spite of Treatment. Presented by DR. SAMUEL AYRES JR.

G. C., a 64 year old white man, was first seen on Dec. 6, 1940, with an eruption on his legs of eight or nine months' duration, beginning as small itchy spots which gradually increased in size. The eruption at that time was limited to the right leg, especially the outer aspect, consisting of discrete and confluent pinhead-sized to half-dollar–sized, violaceous, flat-topped papules and plaques, some with slight scaling. There were no lesions elsewhere.

During the past three months he has received various types of treatment, including a full course of fractional roentgen therapy, two courses of mercury salicylarsenate in 2 cc. doses, totaling twenty-two injections, thirteen injections of bismuth subsalicylate, five injections of calcium thiosulfate, vitamin B complex by mouth, vitamin A by mouth, inunctions of testosterone propionate and local applications of a variety of medicaments, including bland shake lotions, bland ointments and coal tar ointments. While he has been under treatment several new lesions have appeared on the left leg and on one wrist. At one time the eruption seemed to be improved, but the improvement has not been maintained for any length of time.

DISCUSSION

DR. ARTHUR FLETCHER HALL JR.: Although I do not doubt that the man has lichen planus I feel that those larger plaques which are neither infiltrated nor hypertrophic suggest a drug eruption. The patient's wife told me that he took alophen pills (a proprietary laxative containing phenolphthalein) about two or three times a month. Whether that is sufficient to carry the inference of a phenolphthalein eruption or not, I feel there is something in addition to lichen planus.

DR. ANKER K. JENSEN: Many patients with lichen planus respond well to injections of whole liver, and if this has not been given I should give it a trial.

DR. KENDAL FROST: I have a patient who has lichen planus with lesions similar to this patient's. He has had roentgen rays and other therapy and still has the lesions. I think this type of lichen planus is resistant to treatment.

DR. H. C. L. LINDSAY: Arthur Latham suggests small doses of mercury bichloride. He says it is better than arsenic for the treatment of lichen planus.

DR. L. F. X. WILHELM: Have you ever given him bismarsen? I have seen it work when other methods of therapy have failed.

Lichen Nitidus. Presented by DR. SAMUEL AYRES JR.

K. B., a 10 year old white boy, presents an eruption which began when he was about 1 year old and has persisted ever since, with a gradual increase in distribution, although his mother says that the eruption disappeared when the patient was 5 years old, after an appendectomy, and that his skin remained clear for about five months. The mother states that the eruption was mostly on the neck until six months ago, when it began to spread. Previous medication included large doses of vitamin A for the past two months, without apparent benefit, one injection of a bismuth compound two weeks ago and potassium chloride pills.

The eruption is widespread and confluent, extending over a large part of the trunk and neck, down onto the arms and to a less extent on the thighs and legs. The lesions consist of pinhead-sized, flesh-colored, shiny, slightly flattened papules which glisten, giving a beaded appearance as seen on a beaded motion picture screen. On the flexor aspects of the wrists the lesions are less confluent and show typical streaks. There is some scaling on the arms which the patient attributes to a recent sunburn. There is moderate itching.

DISCUSSION

DR. CHRIS HALLORAN: I had a Negro at the hospital with lichen nitidus whom I treated for about a year. No form of treatment altered the disease.

DR. H. C. L. LINDSAY: A patient with resistant lichen nitidus was treated by me for a considerable time, but the disease did not clear up completely until his appendix was removed.

DR. SAMUEL AYRES JR.: Over a period of twenty years I have seen only 3 patients with this disease. One was treated with a bismuth compound and roentgen rays without benefit; another was seen just once and did not come back, and the lesions of the third cleared up with five or six exposures to roentgen rays. If any one treats a patient with lichen nitidus with good results, I should like to hear of it.

Lupus Erythematosus Resembling Érythrose Peribuccale Pigmentaire of Brocq. Presented by DR. MAXIMILIAN OBERMAYER.

C. C., a 28 year old white woman, states that the present eruption on her face began three years ago after a winter vacation in the desert, during which she had exposed herself to the sun as much as possible. It began around the mouth and spread steadily and slowly until it involved the present areas. The intensity of the change in color varies from day to day, and the patient claims that a tingling sensation is present at times. The skin of the face is involved in a fairly diffuse erythematous macular eruption, which is most pronounced on the chin and on the lower part of the cheeks. An area about ½ inch (1.3 cm.) in width around the mouth is spared, a feature which accounts for the perioral pallor. The borders of the eruption are not sharply defined and extend to the center part of the cheeks upward and to the upper part of the neck downward. The color of the lesions is that of a dull erythema with a slightly brownish tinge. On diascopic pressure only the erythematous component disappears and brownish macules are left. She has received a few intravenous injections of sodium succinimide aurate, with some improvement.

Histologic examination of a specimen removed from the left cheek showed the following picture: There was some degree of follicular plugging; there were dilated lymph spaces in the basal portion of the epidermis; the blood vessels of the dermis were dilated, and a considerable amount of perivascular and perifollicular inflammatory infiltrate, which consisted mainly of round cells, was present. A silver stain showed definite hyperactivity in the basal portion of the epidermis in the form of branched melanoblasts.

DISCUSSION

DR. KENDAL FROST: When Dr. Obermayer was sick I saw the patient in the office, and she has improved so remarkably that there is little left of what she had originally. The telangiectasia has almost disappeared, though on careful examination it can be seen. Dr. Obermayer and I had quite a discussion as to the diagnosis.

DR. MAXIMILIAN OBERMAYER: The eruption has somewhat changed under treatment. When first seen it had all the features of érythrose peribuccale pigmentaire of Brocq, namely, plaques of brownish red around the mouth, composed

of erythema and hyperpigmentation and evidenced by the disappearance of the former but persistence of the latter feature on diascopic pressure. Biopsy was performed merely to confirm the diagnosis, and I was surprised to find in the slide the characteristics of lupus erythematosus. In érythrose peribuccale pigmentaire, pronounced vascular dilatation is the only histologic feature seen on ordinarily stained slides. A silver stain, however, revealed definite hyperactivity in the basal portion of the epidermis in the form of branched melanoblasts, a feature which to my knowledge is not commonly encountered in lupus erythematosus but is characteristic of érythrose peribuccale pigmentaire. Thus it may be that the dermatosis which this patient has is a combination of the two diseases.

Monocytic Leukemia with Lesions of the Skin and Mucous Membranes as First Manifestations. Presented by DR. ARTHUR FLETCHER HALL JR.

L. S., a 61 year old white widow, in mid-February 1942 noticed a nontender swelling of the right side of the tongue accompanied by scattered "canker sores." The swelling on the tongue enlarged gradually, and a small ulceration developed near its center; more recently a similar swelling with ulceration was noted on the left tonsil. Late in March small red macules were noticed on the outer aspect of the lower part of the left leg, and on April 1 a large purpuric spot surmounted by a bleb appeared on the left ring finger. About a week ago a hemorrhagic area complicated a slight scratch on the right index finger.

One week ago the right side of the anterior third of the tongue was involved in a large egg-shaped pale pink solid tumor with a shallow punched-out ulceration near its center; the tumor was about 15 by 25 mm. in diameter, discrete and bulging out from the side and above the surface of the tongue. The left tonsil gave a similar appearance and was attended by a small discrete palpable lymph node just below the angle of the left mandible. There were aphthous ulcerations scattered over the buccal lining. The dorsum of the middle phalanx of the left ring finger was completely involved in a purpuric patch surmounted by a large blood-filled bleb; the right index finger showed a purpuric reaction surrounding a shallow scratch. The lower half of the outer aspect of the left leg showed a scattering of uniform lentil-sized purpuric macules.

All of the aforementioned objective findings have regressed in varying degree during the past week but remain obvious enough for identification. Physical examination revealed no enlargement of the liver and spleen and no generalized adenopathy. The urine was normal, and the Eagle and Kline reactions of the blood were negative. A blood count ten days ago showed 3,200,000 erythrocytes and a total leukocyte count of 7,200 per cubic millimeter, with 68 per cent lymphocytes, 9 per cent monocytes and 17 per cent polymorphonuclear neutrophils. The hemoglobin content was 73 per cent. A second blood count yesterday showed 2,760,000 erythrocytes and a total leukocyte count of 15,300, with 75 per cent lymphocytes, 14 per cent monocytes and 13 per cent polymorphonuclear neutrophils. The hemoglobin content was 61 per cent.

Histologic examination of the lesion of the tongue showed changes consistent with monocytic leukemia; the blood smear was also characteristic.

Before the patient was seen by me she received five doses of neoarsphenamine, 0.15 Gm. each, with improvement in well-being but no change in the lesions. During the past week she has received three injections, 15 units each, of liver extract; considerable regression of the lesions has occurred during this time.

DISCUSSION

DR. WILLIAM GOECKERMAN: I accept the diagnosis and have nothing to add.

DR. ARTHUR FLETCHER HALL JR.: I had hoped that this case would bring out more discussion as to the diagnosis. The lesions have faded tremendously;

the lesion on the tongue, which was a fusiform tumor with a definite ulceration in the middle of it, was five or six times its present size. The only treatment she has been receiving is liver extract given intramuscularly, for the anemia. Her white blood cell count has doubled in the last week, increasing from 7,000 to approximately 15,000, with the percentage of lymphocytes rising from 67 to about 75 per cent. Why the lesions should tend to clear in the face of the increasing white blood cell count and the increase in anemia and percentage of lymphocytes is beyond my comprehension.

Book Reviews

Synopsis of Pathology. By W. A. D. Anderson, M.A., M.D., Assistant Professor of Pathology, St. Louis University School of Medicine. Price, $6.00. Pp. 661, including 294 text illustrations and 17 color plates. St. Louis: C. V. Mosby Company, 1942.

It is remarkable that so much information has been crowded into this little volume, considering the great wealth of illustrations. Even references are supplied, and they are up-to-date. Too, the materials are remarkably fresh, with a chapter on the vitamins and inclusion of toxoplasmosis, torula infection and histoplasmosis. The illustrations are excellent, and it is unfortunate that three of the ones in color (facing pages 116, 132 and 334) were apparently forced into the collection; this appears to be a matter of faulty registering of color during the printing.

Criticisms are few. What might appear to be a certain sketchiness is really unavoidable, when one considers the small compass of the book and the great number of illustrations. Information about the acute stage of coccidioidomycosis is missing. The newly discovered spirochete which causes pinta was omitted from the list of pathogenic spirochetes. For the purposes of the dermatologist the section on the skin is too sketchy, but at least it has been made available for the student. The heading on page 95 should read "Tuberculosis" instead of "Virus and Rickettsial Diseases."

The book is attractively bound, compact and well printed on excellent paper. None of the criticisms detract from the general excellence of this up-to-date and otherwise remarkable little book, which so efficiently supplies the high points needed by the undergraduate student of pathology.